FBIS-UST-96-024
21 June 1996

FOREIGN BROADCAST INFORMATION SERVICE

FBIS Report —

Science & Technology

Central Eurasia

Science & Technology
Central Eurasia

FBIS-UST-96-024 21 June 1996

CONTENTS

LIFE SCIENCES

Ukraine: Integrated System for Computer Modeling of Processes of Pressure-Treating Powder Products

964D0598A Kiev POROSHKOVAYA METALLURGIA in Russian No 9-10, Sep-Oct 95 pp 99-104

[Article by O.V. Mikhaylov, Materials Science Problems Institute, Ukrainian National Academy of Sciences, Kiev; manuscript received 16 Dec 93; UDC 621.762]

[FBIS Summary] Until now, the only available software for designing processes for pressure-treating products made of powder has been software designed to operate in a batch mode and to perform isolated tasks. The Materials Science Problems Institute of the Ukrainian Academy of Sciences has developed an integrated graphic tool kit for computer simulation of processes of pressure-treating powder products. The system is designed for IBM-type personal computers, and all its modules have been developed in Microsoft's C. The system consists of a graphic tool environment/shell that users may adjust to their own application problem and a set of numerical-modeling programs that function in the environment. Several programs function under a common interface and may be interchanged by files on an external carrier. The files' structure has been standardized. The programs may be used independently and may also replace analogous user packages. The system's main components are as follows: geographic simulation subsystem; net generator; source data specification subsystem; pressure treatment process simulation subsystem; visual display subsystem; and graphic interface design subsystem. The geometric simulation subsystem may be used to create existing two-dimensional geometric objects of random configuration or edit existing ones by either using a mouse or entering the coordinates of the required points. The real dimensions of the modeling domain may be assigned in a two-dimensional Cartesian coordinate system. The geometric information of the geometric simulation subsystem may be exchanged with an AUTOCAD system through a DXF file. The net generator allows users to automatically plot a net of finite elements. The source data specification subsystem serves to input the initial and boundary conditions of problems of numerical modeling of physical processes by selecting the objects of the finite-element model of a body and entering the required numerical values. Information about the material's physical properties is stored in a database. A separate computer subsystem is used to supplement and correct the information. The pressure treatment process simulation is based on relationships developed within the framework of the theory of the plasticity of a porous body. A rigid-plastic ordered material is considered, and the respective boundary value problems are solved by the finite elements method. A version of the integrated system in which a program for modeling the elastoplastic behavior of the powders of a porous body has also been developed. The visual display subsystem displays the distribution of the study functions whose values are assigned in the nodes of the finite-element model throughout the product's bulk in the form of isolines and isobands. Standard and mixed color pallets are used. Animation effects and three-dimensional representations of the results are also possible. The graphic interface design is used to tailor the system to a specific applications area of the design subsystem and includes a pictogram editor, pictogram menu, pointers (cursors), and fonts. The structure of input and output data may be respecified, and the programs required for solving a given numerical modeling problem may be designated. The operation of the new integrated process design system is illustrated by way of the example of the problem of designing a process for free upsetting of sintered powder cylinders with plane, convex, and concave ends. Figures 6; references 20: 17 Russian, 3 Western.

Russia: Prototype Fully Optical Fiber Memory Described

964D0562 Moscow KVANTOVAYA ELEKTRONIKA in Russian Dec 95 Vol 22 No 12, pp 1,245-1,250

[Article by M.P. Petrov, V.I. Belotitskiy, Ye.A. Kuzin, and V.V. Spirin, Ioffe Physics and Technical Institute, Russian Academy of Sciences: "Fully Optical Ring-Type Fiber Memory for Long-Term Storage, Employing SRS"]

[FBIS Translated Text] *Feasibility of constructing a fully optical dynamic memory based on SRS (Stimulated Raman Scattering) in a fiber lightguide is discussed. Feasibility of employing an SRS-inverter for regeneration of optical signals is examined. Functional properties of the SRS-inverter are investigated theoretically and experimentally. A prototype of a fully optical fiber memory with an SRS-inverter is designed and tested (repetition rate of optical pulses in a fiber loop is 100 MHz, circuit capacity is 500 bits). Pulse circulation was observed for 10 minutes at an average pumping power of 2 W. Speed and energy consumption of devices with an SRS-inverter are also examined, and prospects for improving its characteristics are discussed.*

Introduction

With the increasing bandwidth of fiber communication lines, there can arise the need to develop a buffer storage capable of functioning at the high clock frequencies of the optical pulses it receives. A fully optical ring-type fiber-optic memory may be used as one of possible alternative approaches for such a memory. Its functional

concept is based on circulation of information in a closed fiber-optic circuit as a train of optical pulses with large (logical "1s") and small (logical "0s") amplitudes.

After a prolonged pulse circulation in the circuit, changes inevitably would occur in the pulse shape, amplitude and position with respect to the reference points. Thus, when designing a long-term memory, means must be provided for the pulse reconstruction. Here, the fundamental requirements are: The pulse amplitude, which corresponds to the logical "one" and logical "zero" must remain unchanged; also, there must be no significant pulse shifting with respect to their nominal position and no significant pulse widening. The feasibility of a fully optical pulse regeneration was demonstrated by using a ring interferometer [1] and solitons propagating in the ring [2]. A prolonged pulse circulation was obtained when an inverter based on the SRS effect was used for pulse regeneration [3,4].

A block diagram of the inverter [5-9] is shown in Figure 1. It includes an SRS-amplifier (1), an SRS-oscillator (2), and a spectral filter (3), which pumps the radiation from the amplifier to the oscillator and is responsible for cutting off the radiation at the Stokes wavelength.

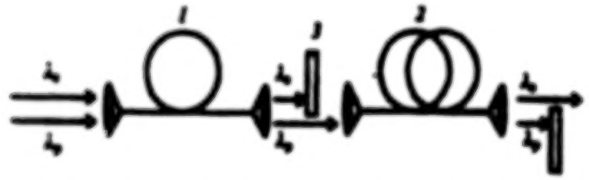


Figure 1. Block Diagram of the SRS-Inverter

When radiation at the wavelength λ_p and the signal pulse at the Stokes wavelength λ_s (logical "one") are synchronously pumped into the inverter, signal amplification and pumping exhaustion occur in the SRS-inverter. Increasing the Stokes pulse at the input causes a greater exhaustion of the pumping pulse, and therefore, the amplitude of the pumping radiation to the SRS-oscillator is decreased. Simultaneously, the filter absorbs the amplified Stokes signal. Thus, the Stokes signal (logical "zero") at the oscillator output is practically absent. In a case when there is no Stokes signal at the input, the excitation radiation passes through the amplifier without being exhausted, it goes through the filter without loss and arrives at the SRS-oscillator. The latter consists of a section of a fiber lightguide, whose length is sufficient for generation of a Stokes signal (logical "one") due to pumping. This is how logical "one" (or "zero") is transformed at the inverter input into logical "zero" (or "one") at the output.

In the performance analysis of devices which employ the inverter, the central problems are the speed, energy consumption, dynamic range, and functional stability. This paper provides experimental data on application of an SRS-inverter in a system of a ring-type fully optical dynamic memory. The stability problem is comprehensively analyzed, and best obtainable characteristics (speed and energy consumption) of the fiber-optic SRS-memory are discussed.

1. Functional Stability of the Optical Memory Circuit With an SRS-Inverter

When estimates are made of the inverter capacity for signal regeneration, properties of the relationship between the Stokes signal output power and the input power are of fundamental significance. When dispersion of group velocities is insignificant, this relationship can be computed from equations, obtained in [10] for an SRS in a fiber lightguide:

$$I_{s,out} = \frac{(I_{s,in} + I_{p,in})\exp[g(I_{s,in} + I_{p,in})z]}{I_{p,in} + I_{s,in}\exp[g(I_{s,in} + I_{p,in})z]} I_{s,in}, \quad (1)$$

$$I_{p,out} = \frac{I_{s,in} + I_{p,in}}{I_{p,in} + I_{s,in}\exp[g(I_{s,in} + I_{p,in})z]} I_{p,in}, \quad (2)$$

where $I_{s,out}$, $I_{s,in}$, $I_{p,out}$, and $I_{p,in}$ are output and input intensities of the Stokes pulse and pumping; g is the SRS gain; and z is the lightguide length. To construct the inverter "input-output" characteristic from (2), we must determine the relationship of the pumping intensity at the SRS-amplifier output as a function of the input signal intensity, and then determine the intensity of Stokes pulse at the output of the SRS-oscillator from (1). If there is no input Stokes signal applied from outside, the triggering Stokes radiation is generated as a result of pumping spontaneous combination scattering. It can formally be accounted for, assuming that an equivalent Stokes radiation with power $h\nu\Delta\nu$, where ν is frequency of Stokes radiation, $\Delta\nu$ is the SRS spectrum bandwidth [11]. For a single mode lightguide at $\Delta\nu = 200$ cm^{-1} this power approximately equals 10^{-6}W.

A sample of the inverter "input-output" characteristic is shown in Figure 2 (curve 1). It was constructed by selecting parameter $g_s z = 10$ for the SRS-amplifier, and $g_p z = 30$ for the SRS-oscillator. We can see from (1), that when I_s is much smaller than I_p the Stokes radiation gain in the lightguide is equal to $\exp(g_p z)$, i.e. the $g_p z$ is an amplification increment at a small intensity of Stokes radiation. With amplification increment of about 16 stokes signal, generated due to spontaneous scattering,

reaches the value equal to half the pumping intensity at the light guide output, which corresponds to the SRS threshold [11]. In this sense, $gI_p z = 10$ corresponds to the below-threshold condition, $gI_p z = 30$ corresponds to the above-threshold condition.

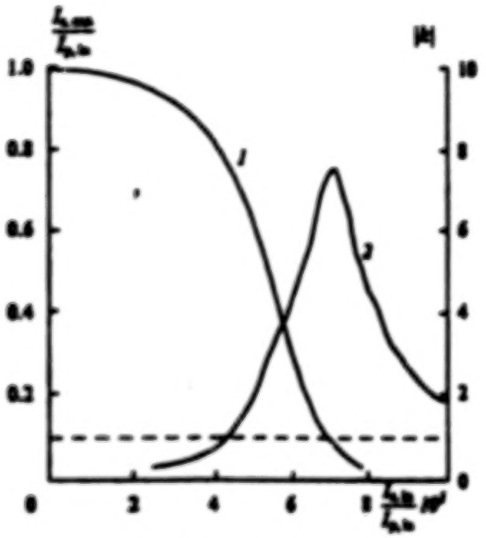


Figure 2. Curves of the absolute value (modulus) of the differential gain and Stokes signal intensity at the SRS-inverter output as a function of Stokes signal intensity at its input.

To provide functional stability (stable circulation of pulses with large and small amplitudes), the inverter "input-output" characteristic must be monotonically decaying and exhibit a differential gain below -1 [12, 8] for $I_{s,min} = I_{s,th} = I_{s,0}$. The value $I_{s,0}$ determines the inverter's switching threshold, and it can vary within a wide range with a linear attenuation (or amplification) of the input signal. Taking into account the latter condition, the differential gain is

$$K = \frac{I_{s,th}}{I_{s,max}} \frac{dI_{s,max}}{dI_{s,th}}; \qquad (3)$$

When $K < -1$, the ratio $I_{s,min}/I_{s,max}$ indicates at which linear attenuation or amplification this value of $I_{s,0}$ will be the threshold value. Modulus K is shown in Figure 2 by curve 2. It is shown that the threshold can vary by a factor of 2.5. In particular, the threshold 7×10^{-5} corresponds to the maximum of modulus K, and $I_{s,min}/I_{s,max} = 10^{-4}$. In essence, this indicates that a very large attenuation can occur in the optical memory circuit.

From equations (1) and (2) we can determine the levels of pulses circulating in the circuit, which correspond to the logical "one" and "zero". The results of this computation are shown in Figure 3. The solid line corresponds to the inverter where the amplification increment in the SRS-oscillator is twice as large as the amplification increment in the SRS-amplifier at identical pumping power. The broken line corresponds to the pulse amplitude of an inverter, which has equal amplification increments for the SRS-amplifier and for the SRS-oscillator. The dot-dash curve indicates a boundary between the intensities, corresponding to the logical "zero" and "one".

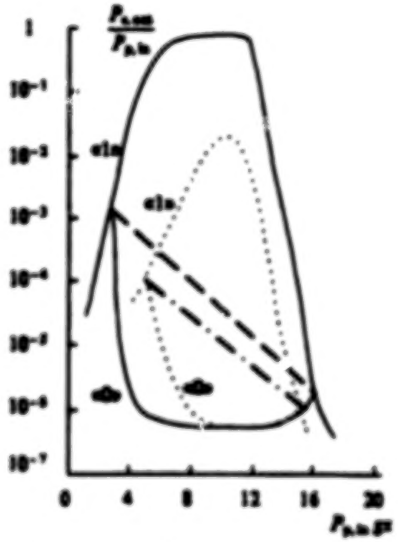


Figure 3. Curves of relative powers of pulses stably circulating in the circuit as a function of the SRS-inverter amplification increment.

From these relationships we can see that the pumping power range with a stable pulse circulation with two amplitudes is quite large. Minimal pumping power approximately corresponds to the level where the total amplification in the SRS-amplifier and SRS-oscillator reaches the threshold level. The maximum power is limited by threshold amplification only in the SRS-amplifier. Computations also demonstrate a very large amplitude ratio of "zeros" and "ones" and a considerable range of allowable level deviations from their steady-state values. This statement is supported by the fact that the random amplitude deviations, for example decreasing by a factor of 1-2 of the pulse amplitude, corresponding to "one", does not remove the pulse from the "one" region. Here, at further circulation, the pulse amplitude will be reconstructing up to its stable value.

"Leakage" of the Stokes wave from the first waveguide into the second greatly affects the inverter characteristic. In this case, the Stokes pulse, which arrived from the first waveguide, instead of spontaneous scattering, must be considered as being the input Stokes signal in the second lightguide. Results of computing stable amplitudes as a function of "leakage" are shown in Figure 4. It was assumed that the SRS-oscillator amplification increment is equal to five, and the amplification increment of the SRS-oscillator is equal to 20. It is demonstrated that leakage of the Stokes radiation at the 10^{-2} level reduces the "zero" and "one" ratio by a factor of three, thus, significantly degrading the inverter properties.

Thus, computations demonstrate that the inverter is capable of maintaining the pulse amplitude, which correspond to logical "zero" or "one," for a long time. The invariability of the mutual time position of pulses and their width is assured, because the signal sequence at each cycle is actually generated anew, and the position and duration of new cycles are tied to the pumping pulses.

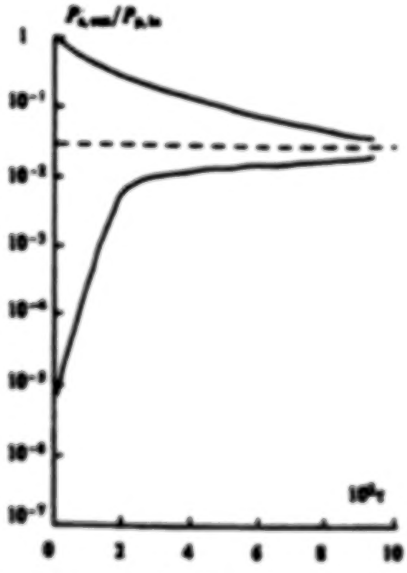


Figure 4. Curves of relative power of pulses stably circulating in the circuit as a function of Stokes radiation transfer ratio from SRS-amplifier to SRS-oscillator.

2. Prototype of a Fiber-Optic Memory With an SRS Inverter

The device shown in the diagram in Figure 5 was used for experimental studies. A YAG:Nd-laser with mode synchronization was used as a pumping source. This laser can generate a continuous pulse train with a duration of about 100 ps, a repetition rate of 100 mHz, and a 1.064 micrometer wavelength. Average radiation power after the optical insulator 9, was 5-7 W. Pumping into the lightguide was provided by a dichroic dielectric mirror 10, and lens 6 with a focal distance of 6mm. The dichroic mirror reflected the pumping radiation with a ninety-seven percent efficiency and at the same time transmitted the signal radiation at Stokes wavelength of 1.12 micrometer with an efficiency of not less than 90 percent. The efficiency of pumping into the fiber was 0.6.

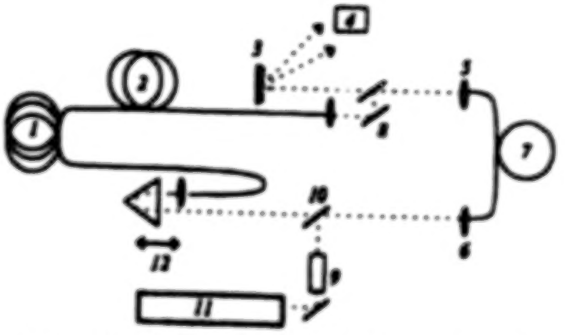


Figure 5. Block Diagram of the Experimental Set-Up.

The SRS-amplifier 7 was made of a section of a single mode lightguide, which maintained linear polarization radiation. The fiber core diameter was 4.5 micrometer. Light attenuation at 1.064 micrometer wavelength was 3.5 dB/km. The lightguide section was selected experimentally to be 22 m, so that the SRS threshold level was 2.5 W of average pumping power. The SRS minimum threshold power of 1.5 W in this lightguide was achieved with lightguide sections longer than 50 m. From the amplifier output, radiation was applied through lens 5 to a spectrally selective filter 8, made of two dichroic dielectric mirrors similar to mirror 10. By performing multiple reflections between mirrors, it was possible to provide a sufficiently large attenuation of Stokes radiation at a near unity coefficient of radiation transmission from a long pumping wave. By varying the number of reflections from mirrors, it was possible to change the leakage coefficient of the Stokes wave from 10^{-1} to 10^{-3}. Efficiency of pumping transmission from the first lightguide section to the second was 0.5-0.6. A portion of pumping radiation, as well as Stokes radiation was applied to diffraction grating 3 and to photodetectors 4.

The SRS-oscillator 2 and delay line 1 were made of a single lightguide section 840 m long, similar to the one used with the SRS-amplifier. Only its small initial

section (50-100 m) effectively participated in generation of a Stokes pulse, while the remaining section was used as a delay line. From the delay line output, the Stokes pulse was applied to the input of the SRS-amplifier through adjustable delay line 12 and a dichroic mirror, thus, closing the loop. Efficiency of the Stokes pulse insertion was 10-20 percent.

The circuit operates as follows. In the initial state, the laser beam is shut off and radiation is not applied to the circuit. After opening the shutter, the pumping pulse train begins to arrive at the SRS-amplifier 7. Because initially Stokes radiation is not present at the SRS-amplifier, and the SRS gain is below the threshold level, the initial pumping pulses pass through the amplifier without depletion. After exiting the SRS-amplifier they are applied to the SRS-regenerator through filter 8 and excite intensive Stokes pulses, which after passing the delay line are applied to the SRS-amplifier by way of the dichroic mirror 10. The variable delay line is adjusted in such a way that the Stokes pulses would agree in time with the following pumping pulses. After the first Stokes pulse has reached the SRS-amplifier, the process changes. The Stokes pulses which arrived at the amplifier input cause pumping depletion at its output and interruption of the SRS-generation. Thus, after a train of intensive Stokes pulses, Stokes pulses with a small amplitude will appear at the SRS-oscillator output.

If the pulse train alternations with large and small amplitude occur as long as desired, this indicates that a stable pulse circulation mode is established in the circuit with two different amplitudes, allowing it to maintain a random signal sequence as long as desired. This mode was recorded in the experiment with a Stokes wave leakage coefficient σ through the filter at a level 10^{-3}. At large γ, we were not able to record a stable pulse circulation of two amplitudes.

3. Experimental Results

An oscillogram of the Stokes pulses envelop at the SRS-amplifier output immediately after switching on laser radiation is shown in Figure 6 (Figure 6 not reproduced). After several gradual oscillations, an almost rectangular meander was observed where the maxima corresponded to the pulse train with a large amplitude, and minima to the pulse train with a small amplitude. Time needed to reach the mode was approximately equal to the laser beam opening time. Power of the Stokes signal with a large amplitude depended on the pumping power, and its peak reached 50 percent of the pumping power applied to the SRS-amplifier. In the best situations, the low level was below the pumping level by at least a factor of 50. In the oscillogram, the signal period, which is equal to the combined width of pulses with large and small amplitudes, was equal to 8.5 μsec. This corresponds to the time it takes light for a round trip in a fiber-optic loop 870 m long. Maximum observation time of stable circulation was limited to 10 min because of technical reasons related to the circuit misalignment. During this time the pulses completed more than 10^8 circulations in the loop. Experimentally measured relationships of the pulse levels with a large and small amplitude at the SRS-amplifier output as a function of pumping power inserted into the SRS-oscillator are shown in Figure 7.

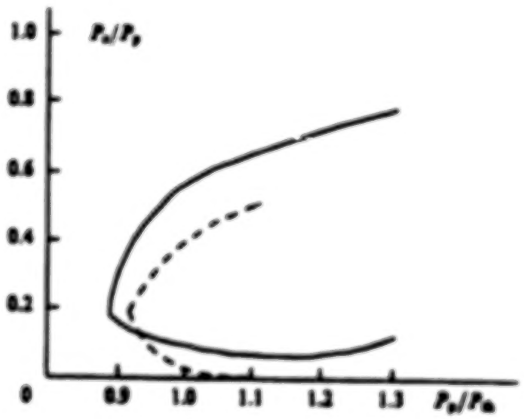


Figure 7. Experimental curves of the levels of pulses with large and small amplitudes as a function of pumping power applied to the SRS-oscillator.

During measurements, the pumping power to the SRS-amplifier was maintained constant at the threshold level for the SRS-amplifier (broken line) or 1.3 times higher than the threshold level (solid line). The experimental relationship is qualitatively similar to the computed one, but disagrees with it quantitatively, because the computations were carried out in approximation of a zero dispersion, which disagrees with the experimental conditions. The dispersion effect on the inverter is most significantly manifested in changes of the pumping pulse exhaustion dynamics when the SRS threshold level is surpassed. When applying rectangular pulses and in the absence of dispersion, a small increase of the threshold level causes an almost complete exhaustion of pumping. At the same time, with a large dispersion of group velocities, only half the pumping pulse energy is re-pumped into the Stokes pulse when the threshold level is exceeded by a factor of two.

The above described results were obtained with an optimal delay in the feedback loop. It was selected experimentally from conditions of minimum pumping power required for developing the mode with two stable amplitudes. Deviation in the delay from the optimum

value caused interruption of the mode with two stable conditions and transition to the mode with one stable condition. Decaying oscillations, gradually changing to a generation of Stokes pulses with a constant amplitude were recorded in this situation. It was possible to restore the generation mode with two stable conditions either by reducing the Stokes wave gain in the feedback loop, or by increasing the pumping power. The curve of the required pumping power as a function of changes in delay is shown in Figure 8. This curve was obtained when 2.8 W of power were applied to the first section, which is greater than the threshold level for this section by a factor of 1.3. Changes in delay within 100 ps caused the required power to increase on the order of 10 percent. The feedback value for all delays was 15-20 percent.

Splitting of the Stoke's radiation spectrum was observed when delay was reduced, i.e. two Stoke's pulses would appear with different frequencies. Longer wavelength component had a frequency shift, corresponding to the maximum of the SRS-amplification for quartz glass.

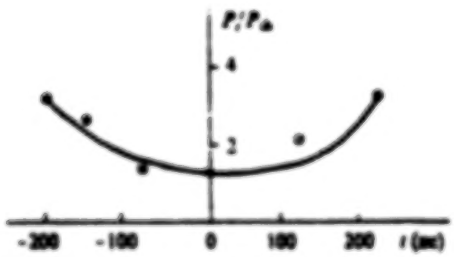


Figure 8. Minimum average pumping power (delivered to the SRS-inverter) providing a bistable circulation mode, as a function of deviation from the optimal delay time in the feedback loop.

The wavelength of the shortwave component decreased with a decreasing delay. Development in time of these two components was different. After the pumping was turned on, the intensity of the longwave component increased relatively sharply, and ceased after a few oscillations. The behavior of the shortwave component was similar to the development of generation in a regular ring laser, when the intensity increases with the radiation circulation in the loop. Oscillograms of Stokes pulses envelops of longwave and shortwave components are shown in Figure 9 (not reproduced).

Generation of two wavelengths in the spectrum of the Stokes component can be interpreted as follows. With a non-zero filter transmission of the Stokes component, its generation in the fiber can occur in one of two ways. Initially, Stokes radiation is developed in the SRS generator from a spontaneous scattering, while its maximum intensity is observed at the wavelength which corresponds to the maximum of the SRS amplification. Next, this radiation is amplified in the SRS-amplifier and is observed in a form of a longwave component. Amplification of the longwave component in the amplifier is accompanied by pumping exhaustion, occasioning a decrease in the component intensity in the following cycle. In this process, each cycle begins with the onset of lasing in a SRS generator, from spontaneous scattering. This process results from the operation of the SRS-inverter and a stable circulation of pulses with two amplitudes.

Alternatively, the Stokes wave in the SRS-laser is developed from the Stokes wave which is leaked from the amplifier through the filter. In this case, it begins gradually to increase with circulation (as in a regular ring SRS-laser). With a gradual development of the lasing during many cycles, the synchronization between the Stokes pulse and the pumping pulse, begins to play a significant role. Under normal dispersion of group velocities, the Stokes long-wave propagate faster and advance to the front. For this identical reason, when the delay in the feedback circuit is decreased, a shorter shortwave component of the Stokes pulse begins to approach the pumping pulse maximum, thereby also providing it with advantageous amplification.

The described processes compete with one another. A generation of a mode with one or two stably circulating amplitudes depends on which of them will be preferred. From the experimental relationships shown in Figure 8, it follows that when the pumping power is increased, this process is the one with two stable amplitudes. It is quite the reverse when the pumping power is decreased. In this case the lasing follows the second alternate version. It is worth mentioning that the type of lasing in the circuit depends on the initial conditions. Thus, for a slower rate of increase of the amplitude of the pumping pulses, when it was turned on, a train of Stokes pulses was generated with a constant amplitude. At the same pumping power, but with a faster rise, pulse trains were generated with two amplitudes.

4. Speed and Energy Consumption of Devices With an SRS-Inverter

In theory, the speed is limited by the minimum pulse repetition period, which in turn must be significantly larger (by an order of magnitude) than the relaxation time of the molecular oscillations (for quartz glass, it is approximately 0.15 ps). Here, the pulse repetition rate could be in hundreds of GHz, and the pulse duration could be approximately 1 psec, i.e. in our experiments,

as well as in computations it can be assumed that the SRS steady-state condition is fulfilled.

When the pulse repetition rate is increased, it causes a rise in the average radiation power, which may lead to more rigid limitations with respect to the pulse repetition rate. It was pointed out earlier that, for the SRS-inverter operation, the pumping power must be near threshold. In the presence of the group velocities dispersion, reduction of pulse duration causes the interaction length to decrease with a corresponding increase in its peak power. It can readily be demonstrated that with this development, the pulse energy needed for generation of the SRS, remains constant and is determined from equation

$$W = 16SD\Delta\lambda/g. \qquad (4)$$

where S is the cross section of the lightguide core; D is dispersion of group velocities; $\Delta\lambda$ is Stokes shift. For λ_0 = 1μm, the dispersion is approximately equal to 40 ps/nm x km [13], the SRS gain is 10^{-11} cm/W, and the threshold energy is equal to 10^{-6}joules/μm². For a typical single mode lightguide, S is approximately equal to 50 mkm² and thus, the average pumping power will be 5 W/GHz.

Studies demonstrated that the reduction of dispersion plays the decisive role in reduction of the threshold power, and consequently in the increase in possible clock frequencies. When the pumping group velocities and Stokes velocity are in agreement, with a pulse width of 100 ps, a lowering of the threshold power is possible by at least an order of magnitude [14]. Here, the effective length of interaction is limited only by the length of the lightguide section (in [14] it is equal to 2.4 km), which assumes feasibility of a further reduction of the average pumping power due to lowering of the pulse width, while retaining their peak power.

Bibliography

1. Whitaker N.A., Gabriel Jr.M.C., Avrammopoulos H., Huang A. Opt. Letts, 16, 1999 (1991).

2. Nakazawa M., Suzuki K., Yamada E., Kubota H., Kimura Y., Takaya M. Electron. Letts, 29, 729 (1993).

3. Petrov M.P., Kuzin E.A., Belotitskiy V.I., Spirin V.V. Pisma to ZhTF, 18, No. 17, 29 (1992).

4. Belotitskiy V.I., Kuzin E.A., Petrov M.P., Spirin V.V. Electron Lett. 29, 49 (1993).

5. Kuzin E.A., Petrov M.P., Spirin V.V. Pisma to ZhTF, 12, 406 (1986).

6. Spirin V.V., Maksyutenko M.A. Kuzin E.A., Petrov M.P. Pisma to ZhTF, 14, 1144 (1988).

7. Petrov M.P., Kuzin E.A., Belotitskiy V.I., Spirin V.V. In Sb. Optical and Digital Image Processing (L. Nauka, 1988, p 135).

8. Belotitskiy V.I., Kuzin E.A., Petrov M.P., Spirin V.V. ZhTF, 58, 1325 (1988).

9. Kuzin E.A., Maksutenko M.A., Petrov M.P., Spirin V.V. Opt. Computing and Processing, 1, 163 (1991).

10. Auyeung J., Yariv A. IEEE J. Quantum Electron., QE-14,347 (1978).

11. Smith R.G. Appl. Optics, 112489 (1972).

12. Gashkovets I., Vasilyeva N.P. Avtomatika i Telemekhanika, 21, 892 (1960).

13. Fleming J.W.J. Amer. Ceram. Soc., 59, 503 (1976).

14. Spirin V.V., Petrov M.P., Kuzin E.A., Belotitskiy V.I. ZhTF Vol. 64 No. 10, p 151 (1994).

Belarus: KF1869VE2 Single-Chip Microcomputer Described

964D0852A Moscow PRIBORY I SISTEMY UPRAVLENIYA in Russian Jan 96 No 1, pp 38-39

[Article by I.N. Antonov, I.A. Yegorov, and I.I. Popravkin, engineers, Integral Scientific Production Association, Minsk; UDC 681.325.5-181.48]

[FBIS Translated Text] The KF1869VE2 universal single-chip four-bit microcomputer is intended for use in creating measuring equipment and systems to control complicated household devices and industrial, medical, and other equipment. It has been manufactured on the basis of high-quality complementary metal-oxide-semiconductor [CMOS] technology. From a design standpoint, it is a flat 64-pin plastic package with four-sided pin arrangement (13 and 19 pins each, spaced at a 1-mm increment, with the package measuring 14 x 20 mm). A type 462.64-2 package has been used.

Figure 1 is a schematic of the [LSI].

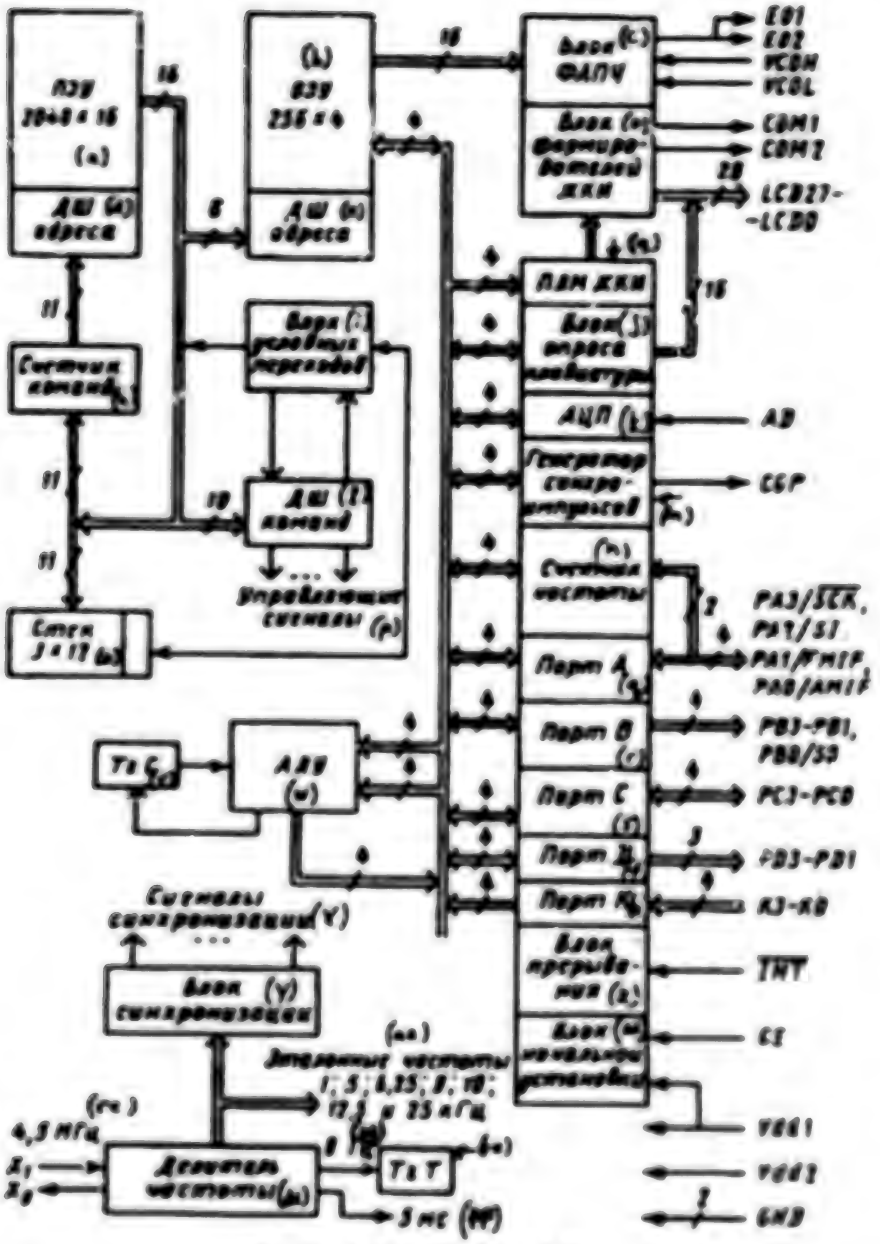


Figure 1. Schematic of the LSI.

Key: (a), permanent memory (ROM, 2,040 x 16); (b) dash memory (RAM, 256 x 4); (c) phased automatic frequency control; (d) address decoder; (e) address decoder; (f) liquid crystal display [LCD] driver; (g) LCD programmable logic array [PLA]; (h) instruction counter; (i) conditional jump module; (j) keyboard-scanning module; (k) analog-to-digital converter [ADC]; (l) instruction decoder; (m) synchronization pulse generator; (n) frequency counter; (o) 3 x 12 stack; (p) control signals; (q) Port A; (r) Port B; (s) Port C; (t) Port D; (u) Port K; (v) transfer flip-flop; (w) arithmetic and logic unit [ALU]; (x) sync signals; (y) synchronization module; (z) interrupt module; (aa) reference frequencies, 1, 5, 6.25, 9, 10, 12.5, and 25 kHz; (bb) initialization module; (cc) 4.5 MHz; (dd) frequency divider; (ee) timer flip-flop; (ff) 5 ms; and (gg) 8 Hz.

The microcircuit includes the following:

—11-bit instruction counter;

—three-level stack;

—four-bit arithmetic and logic device [ALU];

—transfer flip-flop (its counter reset and carry/borrow memory make it possible to perform arithmetic operations over operands with bit lengths that are multiples of 4 bits);

—256 x 4 bit data memory [RAM], 16 cells of which are also general-purpose registers;

—2,040 x 16 bits of masked program storage;

—interrupt module (one level, one input);

—initialization module (after the power supply has been turned on and after synchronization has begun after a wait time on the order of 100-125 ms, the system is reset and the zero-address program that is "protected" in the ROM begins to be executed;

—frequency synthesizer based on a phased automatic frequency control (seven reference frequencies are used, namely, 1, 5, 6.25, 9, 10, 12.5, and 25 kHz, and there are two inputs, namely, VCOL and VCOH, for receiving signals with frequencies up to 30 and 150 MHz, respectively);

—16-bit frequency counter (two inputs, namely, PA0/AM1f and PA1/FM1F, for receiving signals with frequencies of 0.3-5 and 3-20 mHz, respectively);

—programmable sync pulse generator capable of generating pulses with a frequency of 138 Hz to 45 kHz (the CGP contact is the output of the generator or single-bit port), thereby making it possible for the CGP output to be used to feed audio signals (keyboard sonication, signaling of changes in operating mode, etc.);

—built-in six-bit analog-to-digital converter [ADC];

—LCD driver with lead-outs and double multiplexing (a maximum of 56 segments);

—programmable logic array [PLA] of segments (the PLA is programmable with a mask and makes it possible to generate 32 types of LCD panel images);

—keyboard-scanning signal-generation module (a maximum of 64 keys);

—two four-bit input/output [I/O] ports (PA and PC, with the PA port making it possible to specify information I/O on a bit-by-bit basis);

—two output ports (a four-bit port, i.e., PB, and a three-bit port, i.e., PD);

—two two-bit output ports (combined with the LCD control lead-outs);

—four-bit input port, K, to input keyboard signals;

—frequency divider (it produces the processor's internal working frequency of 30 kH, the reference frequencies for the phased automatic frequency control module, an 8-Hz signal to set the timer flip flop, and a 200-Hz signal to count time intervals);

—built-in timer flip-flop (it is set every 125 ms and reset by a testing instruction, thereby making it possible to achieve clock and time interval-counting functions by means of software);

—built-in serial eight-bit interface (the PA2/S1 is the serial data input contact, the PB0/S0 is the serial data output contact, and the PA3/SCK is the shift synchronization contact during I/O);

—halt mode control module (which makes it possible to set up the microcircuit's operation in a microconsumption mode).

Key Specifications:

Clock frequency, MHz	4.5
No. instructions	95
Instruction execution time (computer cycle), μs	33.3
Supply voltage, V	5 +/- 10 percent
Current consumption:	
when CPU and phased automatic frequency control are operating, mA	≤25
when CPU and the inhibit circuit of phased automatic frequency control are operating, mA	≤0.65
in storage mode, μA	≤10
Range of operating temperatures	-10 to + 70

Authors' address: 220064, Minsk, NPO Integral. Phone: (0172) 78-31-98.

Russia: Urals Telecom Network Undergoing Digitization

964D0764 Moscow VESTNIK SVYAZI in Russian Feb 96 No 2, pp 38-39

[Article by B.F. Shusherin, general manager, AOOT UralTelekom, Sverdlovsk Oblast; V.K. Panov, general manager, Yekaterinburg Telephone Exchange; and V.G. Karpenko, general manager, IskraUralTEL joint venture: "Digitization of Ural Communications Network"]

[FBIS Translated Text] According to the "Concept of Russian Federation Development in the Communications Field to 2010," it will be necessary to have 33.6 million and 4.38 million switching equipment units for Russia's urban and rural communication networks, respectively. The organization of reliable telephone communications at all levels of the Interconnected Communications Network (ICL) of Russia is provided by the joint venture (JV) IskraUralTEL. For construction of long-distance AMTSs [automatic long-distance telephone exchanges] and urban ATXs [automatic telephone exchanges] the joint venture uses certified systems ESWD by Siemens (Germany) and IskraTel (Slovenia), as well as SI 2000 by IskraTel for urban and rural ATXs.

The JV entered the digital communications systems market in 1991, when manufacturing of SI 2000 systems was launched at the Ural Electromechanical Plant (UEMZ, the city of Yekaterinburg) in cooperation with a Slovenian company IskraTel. Soon after, the Ministry of Communications of Russia issued a compliance certificate (N 5-24 Yu-SI of 30 April 1992) for all SI 2000 equipment, which for many years has been used in country's power systems. Also in 1992, a contract was made with the State Customs Committee (GTK) of Russia for organizing an SI 2000 systems-based Russian customs communication network.

Joint Russian-Slovenian enterprise "IskraUralTEL" was officially registered at the beginning of 1994. The JV founders were UEMZ (Yekaterinburg, Russia), Russian joint stock company "YeES Rossii" (Moscow, Russia), IskraTel (Kran, Slovenia) and Teling (Kran, Slovenia).

Yekaterinburg-made equipment SI 2000, which has presented itself in good light in Moscow, Sochi, Ivanovo, Novosibirsk, the Transbaikal Region, Primorskiy kray, the Sakhalin Island and the Urals, first appeared in 1988. Then, a small 540-connection point branch exchange SI 2000/124 was installed at the Joint Dispatch Administration (ODU) of Ural Power Systems. Even today the exchange works perfectly well under rather specific conditions, because a dispatcher connects to it at the subscriber level and has constant, reliable communications with the entire Ural power network even in the case of a higher load.

Later, JV specialists began exchange installation in a number of towns in the Sverdlovsk, Chelyabinsk, Perm, Orenburg and other oblasts in Russia, while constantly finding new partners, providing high-skilled technical support for them and solving practically all problems of organization of communications.

Adaptation

It is well known that Russian communication networks use three-wire (incoming and outgoing) connecting lines (CLs), while the European standard provides for using universal two-wire CLs. And although there are "converters" of three-wire CLs in certain foreign switching systems, e.g. Coral (Tadiran, Israel), most of them only have digital terminals. But system SI 2000 exchanges interface with all types of lines used in Russia and CIS countries — analog (urban three-wire long-distance single-frequency) and digital (one-and two-bit) lines, as well as rural transmission systems V-2, V-3, KNK-6, KNK-12 and IKM-15, which have practically become the standard for rural networks. No foreign exchange fits in Russia's urban, rural and departmental networks as flexibly as SI 2000, which has the R2 signaling system widely used in Europe and provides interface with cellular and trunk systems. For instance, in Rostov-Na-Donv and Novgorod an SI 2000 exchange is used for interfacing with Motorola and Siemens cellular systems.

Service

One can operate an SI 2000 exchange without the permanent presence of personnel (no regular preventive work is needed), by observing and controlling one or several exchanges from a remote operations and maintenance center (OMC) via the existing telephone network.

An OMC operator and operator of an exchange communicate in the MML language (Man-Machine Language) according to CCITT recommendations. OMC software stipulates a network of high-efficiency workstations (Unix) and a large number of support tools. As a terminal that controls exchange operation one currently uses a personal computer. Professionals who were trained at the JV training center work on a PC completely independently, changing parameters of line facilities and subscribers and types of signaling systems, solving problems of providing various services etc.

Operation of the exchange has proven high hardware and software reliability according to CCITT requirements and recommendations. Cases of failure of certain

components were caused mainly by incorrect operation or external inputs that had not been covered in original specifications. For instance, in the town of Kachkanar, where storms are a frequent occurrence, additional external protection on a cross had not been ordered, and during the next storm several boards failed.

Equipment reliability combined with a small inventory of boards (under 20 types) and modules used makes it possible to form optimum spare parts kits. A kit size is determined by the distance to the installation and customer's requirements.

Currently IskraUralTEL offers a new version, V4.4, of systems SI 2000, which has more functional capabilities and better operating characteristics. SP specialists convert existing exchanges to the new version without changing the hardware.

Digital Network Expansion

Three SI 2000 exchanges — central, southern and northern — have been installed in the town of Asbest. They are interconnected by digital the radio repeater transmission systems "Radan," which were tuned jointly with Izhevsk Radio Manufacturing Plant specialists. There are no permanently present personnel at the Southern and Northern exchanges; control, diagnostics and maintenance of the exchanges are provided from the central exchange.

In November 1994, JV specialists installed and commissioned an SI 2000/224 rural exchange drops with 2600 terminal points at the settlement of Isetskoye (Tyumen Oblast). Here for the first time one had to organize systems with standard terminal equipment of rural and rural-suburban ATXs, transmission systems IKM-15, "Radan-2," V-2 and V-3, as well as mini-RRS [radio repeater system] "Malyutka"; the latter has caused the most problems. This exchange also interfaces, via line equipment 1 VCh (2600 Hz) and an analog-to-digital converter (ADC), with Tyumen AMTS of the ESWD type. An "intelligent" signaling converter SI 2000/814 by IskraTel is used as the ADC.

During installation of a small S-2000 regional exchange with 2210 terminal points in the settlement of Zarechnyy, JV professionals have encountered the problem of interfacing with three-wire universal signaling equipment and are implementing there digital universal signaling equipment for a more optimum connection (via digital transmission lines) to the exchange environment.

At the Yekaterinburg GTS [urban ATX], the first SI 2000/224 exchange installed in the Moskovskaya Gorka area was commissioned in two stages — in January and March of 1994. Only three-wire terminations were used for interfacing with the analog environment; later it is planned to use digital transmission lines, too. The Moskovskaya Gorka exchange operates completely autonomously, i.e. without the permanent presence of operating personnel. Some time ago subscribers began complaining about audibility. It has turned out that during the design stage one did not take into account the large number of intermediate stages with high attenuation levels. These drawbacks were eliminated jointly with the city network personnel. At present the exchange operates reliably, and the network management has made a decision to expand the GTS using this equipment.

An SI 2000/224-based pful tandem switching point KU-59 with 2640 digital CLs which was installed in Yekaterinburg in order to relieve the long-distance telephone exchange MT-20 has been operating rather successfully for a year. This is the first debugged version of the last 4.4SX version, which was originally designed for a higher load because a lot of departmental exchanges with various signaling systems are connected to the switching point.

The SI 2000 exchange installed at ATS-65 in January 1995 is the largest in Yekaterinburg, with the rated capacity of 10,000 subscribers. Three more such exchanges will start operation in the city in the immediate future.

All SI 2000 exchanges connected as departmental ones also have been operating reliably, although they are used in networks with diverse signaling systems - 3W ADASE, 2 VCh (1200 and 1600 Hz), three-wire CLs with an M 60 switch etc. and perform a lot of additional functions (dispatcher-dispatcher, dispatcher holding, all kinds of through traffic etc.)

After an SI 2000/124 exchange, which had presented itself in an excellent light, was installed in the Ural ODU, the equipment was commissioned at the UEMZ. Although as far as numerous technical and functional parameters are concerned this system, the last Version II system installed by the JV, is inferior to a Version IV system, it has been operating faultlessly.

Now, a SI 2000/224 exchange with 2600 terminals was commissioned in two stages at the Verkh-Isetskiy plant. It performs the functions of a departmental exchange, but of course without signaling typical for a departmental network.

The majority of Ural power systems — Sverdlovenergo, Permenergo, Tyumenenergo and Orenburgenergo — are equipped with SI 2000/124 V4.3. All exchanges are connected into a loop by transmission systems with double-frequency signaling equipment. Up until recently, due to the fact that the power industry personnel uses the 1200

and 1600 Hz frequencies, voice spectral components of voice caused false activations and malfunctions. JV specialists modernized the software, and the problem has been solved.

JV specialists provide comprehensive personnel support, perform analysis and measurements and issue recommendations necessary for successful exchange operation. When strong EMI began affecting the operation of a large departmental SI 2000/124 exchange installed at the Main Administration of the Russia Tsentrbank, deteriorating transmission quality and causing dumping of communications, JV professionals identified and eliminated the source of interference. It is well known that an SI 2000/124 telephone exchange is a state-of-the-art digital automatic multimodule SPC (Stored Program Controlled) system with distributed control, which supports all major telephone functions (local, incoming, outgoing and through-traffic communications), as well as a large number of additional services (call forwarding, incoming/outgoing call blocking, conference calling, intercepting malicious calls etc.)

Maximum capacity	18000 ALs [subscriber lines] or 3720 CLs (analog or digital)
Number of routes	512
Total capacity	3000 ERLANG
Capacity	100,000 calls in busy hours
Power consumption	0.5-0.9 W per subscriber line
Overall dimensions of the rack	1900 x 440 x 696 mm
Mass	280 kg
Stable operation at +5 to +40°C and 20-80 percent humidity	

Digital hardware and software configuration makes it possible to expand flexibly and change technical solutions and functional capabilities of the system in accordance with state-of-the-art technology and component base.

Connection of any module to a digital communications field takes place via an PCM channel at 2 M6 (G703 CCITT, NDB3 code), with the possibility of using standard transmission equipment and optimum placement of modules (at the ATX proper or on extensions).

The system is based on a Motorola microprocessor (from an 8-bit MC 68B02 to a 32-bit 68020), state-of-the-art component base (signaling microprocessor DSP6001, IKM controller Siemens SAB82525, XILINX XC3020 etc.) and H-CMOS logic ICs. The software is organized at three levels — system software, application software and semi-permanent data (SPD). The application software uses the program-modular principle.

IskraUralTEL is offering turn-key equipment SI 2000. Part of the equipment is manufactured at the UEMZ. Detailed engineering documentation and software are developed and equipment is installed and debugged by IskraUralTEL Russian specialists. All technical and operating documentation is in Russian. Operating and maintenance personnel training is conducted for two to five weeks by Russian specialists at the JV training center.

The technical support center, located in Yekaterinburg, provides service, warranty and post-warranty service of ATX SI 2000.

Russia: 'Kvant-E' Automated Telephone Exchange Described

964D0765 Moscow VESTNIK SVYAZI in Russian Feb 96 No 2, pp 41-42

[Article by V.O. Zhoglo, chief designer of ATX "Kvant-E," and V.K. Staritsyn, first vice president, Moscow Digital Telephone Company joint stock company: "Domestic 'Kvant-E' ATX"]

[FBIS Translated Text] The "Kvant-E" electronic digital automated telephone exchange (ATX) was developed according to Ministry of Communications of Russia specifications; it meets main provisions of the Interrelated Communications Network and has compliance certificates for rural and office-production exchanges. After successful completion of tests of an urban ATX "Kvant-E" in the town of Volgodonsk, compliance certificate No. OS/1-G-54 for an urban exchange with a capacity of up to 100,000 numbers was received. Certification tests of ATX "Kvant-E" as an AMTS [automatic long-distance telephone exchange], a zone hub and a special services hub.

The Moscow Digital Telephone Company (MTsTK), which includes ATX "Kvant-E" developers, equipment manufacturers - AO "Sokol" (Belgorod), AO "Impuls" (Moscow) and AO "VEF-KT" (Riga) - and installation and debugging organization AO "MTU Saturn" (Moscow), is actively promoting ATX "Kvant-E" onto the Russian market. A head service center is being organized at "MTU Saturn." Regional centers are being organized in Yekaterinburg, St. Petersburg, Samara, Chelyabinsk, Novosibirsk and Krasnodar, and software generation centers are being organized in Moscow and St. Petersburg.

MTsTK activity was approved by GKES of Russia in Resolutions No. 99 of 28 December 1994 and

No. 139 of 20 December 1995. A series of multi-purpose ATXs "Kvant-E" was commissioned in 1995: urban ATXs in Volgodonsk (Rostov Oblast) — 4,000 numbers, Saratov — 1,000 numbers, Noyabrsk (Tyumen Oblast) — 600 numbers, Raduzhnyy (Vladimir Oblast) — the central ATX, and Yurga (Kemerovo Oblast) — a rural-suburban hub; office-production ATXs in Moscow (the Ministry of Foreign Affairs — 600 numbers), Kaluga (power industry departmental network — 600 numbers), Kandalaksha (Murmansk Oblast) — Ministry of Railways hub network, and Vologda ("Rostelekom" joint stock company network — 400 numbers); and a large number of small ATXs with 100-200 number capacity.

The ATX equipment is installed in constructive "Yevropa 3"; it consists of TEZs, magazines, modules, racks and rack rows. Overall dimensions of a rack are 2100 x 600 x 450 mm. TEZ dimensions are 280 x 233.5 mm.

A 100-number ATX is a module enclosed in a protective housing 600 x 500 x 400 mm. A 2000-number ATX with digital CLs [connecting lines] is a row of four 2400 x 500 x 2100 mm racks. A 10,000-number ATX with digital CLs consists of five four-rack rows with the square area not exceeding 45 square meters. (Typical ATXs are shown on the inside front cover).

Basic Technical Parameters

Subscriber capacity	100 to 10,000 numbers
Specific load per subscriber line	up to 0.2 Erl
Number of CLs	up to 20,000
Specific load per CL	up to 0.8 Erl
Primary voltage	minus (54-72) V
Power consumption per AL	1 W
per analog CL	2 W
per digital CL	0.5 W
Operating temperature	5 to 40°C
Relative humidity	80 percent at room temperature
Specific load due to equipment	not to exceed 450 kg/m^2

All ATXs are designed individually per customers' specifications.

Flexible configuration and distributed control system make it possible to use ATX "Kvant-E" efficiently for developing digital communications networks for urban and rural regions. In the center of a network one installs a reference-transit (OPTS) exchange — an automatic switching hub connected via digital communications lines PCM-30 (pulse code modulation) or PCM-120 with terminal ATX "Kvant-E" with a 100-2000 numbers capacity. OPTSs are connected to the region's central ATX or an existing central ATX is connected to a new ATX "Kvant-E," which takes over the function of the central ATX. Small overall dimensions of ATX "Kvant-E" make it possible to install the central and terminal exchanges in individual rooms or apartments in residential housing.

To create digital transmission lines in rural and especially urban settings it is expedient to use small-size radio repeater lines [RRLs] "Pereval-1" and "Pereval-2" developed and manufactured by AO "Impuls" (Moscow). The ATX "Kvant-E"-RRL "Pereval" interface is done with a four-wire cable with no additional devices. Simple calculations demonstrate that at distances as low as 1 km it is more advantageous to use RRLs rather than cable lines.

ATXs "Kvant-E" interact with all types of existing and new ATXs in Russia and CIS countries; they use various types of signaling and operate via physical connecting lines and channels of transmission systems with frequency and pulse-code signal modulation. When using transmission systems with PCM, ATX "Kvant-E" is connected to a group channel. Communications between same-type ATXs is established via a common signaling channel, without intermediate equipment.

The ATX provides:

flexibility in expanding its capacity and increasing its carrying capacity;

an open and closed numbering system with any number length;

interaction with other ATXs for all types of CL sets;

transmission of control signals by all methods;

organization of bypass communication routes;

cost accounting of all local and long-distance calls;

distribution of subscriber lines among 16 categories;

connection of pay phones for local and long-distance communications;

organization of dispatcher communications;

fire and security signaling systems for premises;

connection of subscriber lines via a blocking device;

a central operations and maintenance system;

cost rating of additional services;

and a system of operative investigative measures (SORM).

The following services are provided for subscribers:

all types of telephone communications, including long-distance and international communications;

equipment with frequency-dialing capability;

a high-quality voice channel;

and communications with radio subscribers via "Altay" radio station.

Main additional services:

a permanent number;

caller ID;

caller ID records;

records of outgoing long-distance calls;

speed dialing;

direct communications;

call-back;

call forwarding during conversation;

outgoing notification call;

incoming notification call;

information during conversation;

temporary call forwarding;

night service;

temporary inhibition;

temporary selective restriction;

reminder;

and conference calling.

From the start, series production ATX "Kvant-E" has been constantly improved to increase its operating reliability, expand functional capabilities, reduce operating expenses, and create additional comfort for operating personnel. All equipment modifications can be made to quasi-electronic ATXs made earlier. This approach makes it possible to maintain these exchanges at the state-of-the-art technical level.

Small ATXs have a built-in power supply operating from a 220 V 50 Hz a.c. line.

Maintenance of ATX "Kvant-E" is fairly simple and inexpensive, due to the modular configuration, redundancy of station-wide devices, presence of an intrastation diagnostics and control system and development of regional maintenance centers.

The steps that have been taken make it possible to ensure:

implementation of automatic control and diagnostics of the equipment and detect equipment failures accurate to one functional module;

automatic lockout of faulty equipment;

simple changing of subscriber data and code numbering;

automatic recording of telephone traffic parameters;

the use of a PC during maintenance;

automatic checking of time intervals of dial parameters;

and all maintenance functions that can be performed from operations and maintenance centers covering individual regions (oblasts).

There is no need for constant maintenance — the equipment is under constant observation by the intrastation diagnostics and control system. The quality of ATX operation can be controlled from the operations and maintenance center equipped with ATX "Kvant-E" equipment.

AO "MTsTK" supplies, installs and puts ATX "Kvant-E" in operation on a turn-key basis. The ATX warranty period is 1.5 years, approximate cost is $125 per subscriber line (without taking into account the NDS [value-added tax]). The cost depends on exchange configuration, therefore the price is calculated after receiving customer's specifications. Per customer request the ATX can be equipped with a power supply and anode-cross-connecting device. Small (up to 200 numbers) ATXs are sold on a 100-percent prepayment, larger ones — on a 60-percent prepayment. The shipping and commissioning date depends on the ATX capacity but does not exceed six months.

Ukraine: Development of Non-Oxide Ceramic Materials Based on Silicon Carbide and Silicon Nitride

964D0486A Kiev POROSHKOVAYA METALLURGIYA in Russian, Nos 7-8, Jul-Aug 96 pp 24-32

[Article by G.G. Gnesin, Institute of Problems in Materials Science at Ukrainian National Academy of Sciences, Kiev; UDC 621.762]

[FBIS Summary] Since the study of ceramic refractory materials with a covalent chemical bond had began in the mid-1950s by Academician I.N. Frantsevich (1905-85) and Professor G.V. Samsonov, there have been developed several composite materials on either a SiC (α-phase, β-phase) or Si_3N_4 (α-phase, β-phase) rather than oxide base. Either of the two silicon compounds ensures low defect concentration and mobility at high temperatures (1700-2100°C) along with excellent thermomechanical and electrophysical properties. Considering that diffusion of atoms of nonmetallic refractory compounds is very slow and sintering their powder mixtures is very difficult, there have been devised six special methods of controlling the structurization process and thus obtaining either nonporous materials or not exceeding specified porosity levels. They are: 1. mechanical activation of ultrafine-disperse powders, 2. sintering aided by the gaseous phase (sublimation - dissociation - condensation), 3. liquid-phase sintering (diffusion - recrystallization through melt), 4. sintering under pressure (hot pressing or hot isostatic pressing with diffusion, diffusive-viscous flow, formation of secondary phases), 5. reactive (chemical) sintering aided by the liquid phase (heterogenous interaction producing secondary phases, reactive diffusion, topochemical reaction), 6. reactive (chemical) sintering aided by the gaseous phase. Activation of the sintering process can be achieved in powders with a thermodynamically off-equilibrium structure or by dissolution of foreign atoms resulting in creation of nonstoichiometric states. Most effective activators are additives which form oxynitride solid solutions with a wide homogeneity range in Si-Me-O-N systems (Me: alkaline-earth metal or rare-earth metal), also Al,Ga,Zr,Y,Be,Mg oxides. The sintering process speeds up when powder particles become simultaneneously alloyed with additive particles by way of diffusion, homogenization then being attended by a rising concentration of atomic vacancies and rising stresses. Now, since the early nineteen eighties, are being studied the effects of structural features and defects particularly in polycrystalline ceramics on the physical and performance characteristics of these materials as well as on their interaction with external media and fields. For illustration are presented data on Si_3N_4 ceramic with a) 4-85 vol.% TiN, b) 30 vol.% SiC fiber, c) 20 or 30 vol.% C fibers, d) 10 or 30 vol.% SiC whiskers, the characteristics of each composite material depending on the volume fraction of the filler as well as on the sevice temperature. Figures 4; tables 3; references 45.

Ukraine: Composite Materials for Contacts and Electrodes: Review

964D0486B Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 32-53

[Article by R.V. Minakova, M.L. Grekova, A.P. Kresanova, and L.Ya. Kryachko; Institute of Problems in Materials Science at Ukrainian National Academy of Sciences, Kiev; UDC 621.762]

[FBIS Summary] Development of composite materials for electric contacts in switching devices and for electrodes in a variety of devices ranging from comunication apparatus (μA,μV range) to low-voltage or high-voltage (kA,kV range) power apparatus began in the nineteen fifties under the guidance of Academician I.N. Frantsevich (1905-85). Any set of performance characteristics not realizable with one metal has been found to be realizable within pseudoalloys of Ag(Cu,Ni) with refractory W(Mo,Cr). Powders of metals are mechanically mixed, sifted, and alloyed. Oxides and other compounds are mechanically mixed and chemically precipitated, then concurrently reduced to metals. Contacts and electrodes are produced from pseudoalloy powder mixtures by any of the four available molding technologies: 1. hot pressing (hot isostatic pressing) with or without supplementary thermomechanical treatment; 2. solid-phase sintering with additional pressure treatment followed by annealing and then supplementary pressure-temperature treatment; 3. liquid-phase sintering followed by additional pressure (extrusion, rolling) or ultrasound treatment and subsequent annealing; 4. bimetal (blank and sublayer) pressing with or without subsequent heat teatment above the pour point, followed by pouring and formation of contact or electrode holders, with or without subsequent pressure, heat or ultrasound treatment. The final treatment is machining to precise dimensions. Various admixtures to the basic composite material will enhance certain properties: B,BN,C improve the spreading and the wetting; MoS_2,BN,C lower the friction coefficient; CaO,LaB_6, Y_2O_3 raise the emissive power.The report covers results of extensive research done on the subject and published over the 1961-91 period. It includes data on the structurization and the ultimate microstructure of the thus produced materials. It also includes data on their essential characteristics: 1. dependence of electrical conductivity (cathode, anode) and erosion rate as well as of mechanical impact strength on the porosity and on the

electric current density; 2. dependence of the change of both cathode mass and anode mass during the three preinversion-inversion-postinversion stages on the arc current, on the arc duration, and on the material composition. Figures 8; references 47.

Ukraine: Structural Factor in High-Pressure Synthesis of Superhard Phases

964D0486C Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 83-92

[Article by A.V. Kurdyumov, Institute of Problems in Materials Science at Ukrainian National Academy of Sciences; UDC 548.33:539.26]

[FBIS Summary] Forward phase transformations of crystalline boron nitride and carbon under high pressure during superhard phase "synthesis" are analyzed on the basis of scientific research done and published over the 1964-94 period. Noteworthy is the analogous polymorphism of these two substances, as indicated by their almost coinciding or at least similar theoretical pressure-temperature phase diagrams extending to temperatures above 4000 K and pressures above 15 GPa. The two basic forms of both graphite and boron nitride in the laminar trigonal class are their hexagonal and rhombohedral ones, while in the tetrahedral class sphaleritic and wurtzitic forms of boron nitride compare with cubic diamond and its hexagonal lonsdaleite allotrope respectively. Only hexagonal graphite and cubic diamond, hexagonal and sphaleritic boron nitride, and the liquid phases of both substances are stable - each within a particular region of the P-T diagram. The phase transformations of the two substances differ, however, which is important from the technological standpoint. The two BN_{hex}(stable) → Wur(metastable) and $graphite_{hex}$ (stable) → lonsdaleite(metastable) transformations proceed according to the martensitic mechanism only, but then the kinetically irreversible lonsdaleite → diamond(stable) and Wur → Sph(stable) transformations proceed differently: the former also according to the martensitic mechanism and the latter according to the diffusion mechanism. Of practical interest concerning the technological aspect is that the rhombohedral phases can be transformed either into the metastable hexagonal ones (lonsdaleite, wurtzitic BN) or into the stable cubic ones (diamond, sphaleritic BN) whose hardness may exceed 50 GPa Vickers. Experimental studies have revealed a strong effect of structural imperfection in the stable initial phases on their transformation, under high pressure, into metastable ones. Most detrimental during static compression and much more so during shock compression are turbostratic defects, which cause one-dimensional disordering in the initial phase and so along with three-dimensional disordering lower the volume fraction of the metastable phase. Presence of water has been found to significantly offset the effect of such a structural imperfection. Figures 7; references 38.

Ukraine: Elasticity Constants and Moduli of Cubic and Wurtzitic Boron Nitride

964D0486D Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 92-99

[Article by A.V. Bochko and O.I. Zaporozhets, Institute of Problems in Materials Science and Institute of Metal Physics at Ukrainian National Academy of Sciences, Kiev; UDC 621.762]

[FBIS Summary] Abrasive knives made of superhard sintered boron nitride (Hexanite-R, R-cutting tool grade) in an organic binder with antifriction additives have been developed at the Design and Manufacturing Engineering Office (Institute of Problems in Materials Science) and are being produced at the Poltava Diamond Manufacturing Plant, namely special-purpose knives for sharpening of tools made of high-speed and quenched steels. The scientific basis of this development is the W.Voigt-A.Reuss- R.Hill strain energy theory and calculation of elasticity moduli and other constants according to Hill's extension of this theory for single crystals to isotropic polycrystals. Thus had been calculated the four basic parameters: 1. Young's modulus E, 2. shear modulus G, 3. bulk modulus K, 4. Poisson's ratio, also both longitudinal and transverse speeds of ultrasound. The theoretical study was supplemented with an experimental one for verification by mechanical testing. The specimens of Hexanite-R represented four stages of the Wur (wurtzite) → Sph (sphalerite) transformation: 1. 80% Sph + 20% Sph, 2. 50% Wur + 50% Sph, 3. 40% Wur + 60% Sph, 4. 100% Sph. For reference and comparative evaluation were also used data on three commercial grades: 1. Elbor-RM (100% Sph), 2. Kiborit (98% Sph + 2% AlN,AlB_{12}, 3. Elbor-R (% Sph + 3% AlN,AlB_{12} . Tables 4; references 21.

Ukraine: High-Temperature Composite Materials

964D0486E Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 140-149

[Article by Yu.L. Pilipovskiy, L.G. Vishnevskiy, T.V. Grudina, and L.N. Pereselentseva, Institute of Problems in Materials Science at Ukrainian National Academy of Sciences, Kiev; UDC 621.762]

[FBIS Summary] A theoretical and experimental study of heat-resistant composite polymer-carbon materials

was made at the Institute of Problems in Materials Science concerning their erosion resistance in streams of hot gas-condensate mixtures and the development of a new technology so as to maximize that resistance. As a way to achieve this, it has been proposed to: 1. use thick reinforcing carbon (coke) elements as filler in a readily deformable multidimensional polymer layer with a raised surface, which should produce an almost homogeneous material having not only a 2-3 times higher shear strength but also an immunity to parting and local wear; 2. insert refractory metal filaments into the reinforcement structure so as to better retain the reinforcing coke by formation of chemical bonds at the interphase boundary and raise the thermal conductivity at the microscopic level. In the experimental part of the study specimens of polymer matrices with strips of carbon cloth (1.3-1.5 mm thick, 2.0-2.5 mm thick, 4.0-4.5 mm thick) or with tricot sheets, with strips of carbon+glass cloth (3.5-4.0 mm thick) or with tricot sheets, and with strips of carbon+ metal cloth (4.5-5.0 mm thick) or with tricot sheets were mechanically tested for percentage elongation and breaking stress under longitudinal and transverse loads. In the theoretical part of the study has been constructed a mathematical engineering model for design and performance evaluation of heat-resistant composite materials, which include also ones containing pseudoalloys such as those of the W-Cu type or carbides. At this time is being studied the feasibility of lowering the density of heat-resistant composite materials and making them more effective thermal insulators by use of organic reinforcing fibers. Figures 7; tables 2; references 10.

Ukraine: Physicochemical Transformations in Ablation Layer of Thermal Protection Materials

964D0486F Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 149-160

[Article by V.N. Bulanov and A.A. Korol, Institute of Problems in Materials Science at Ukrainian National Academy of Sciences; UDC 678:621.762:536.3:536.49]

[FBIS Summary] Studies of physicochemical transformations in thermal protection materials for space flight have been made, their possible effect on abalation of these materials in the condensed state is a major concern. Conventional materials for this application are composite ones which consist of phenolformaldehyde resins such as Bakelite as the binder and glass-plastic, glass cloth, or carbon-plastic as the reinforcing filler. Their capacity to absorb heat during transition from condensed to gaseous state is a measure of their thermal effectiveness. An analysis of both attendant structurization and relaxation processes involved in the dynmics of physicochemical transformations, an analysis based on a numerical solution of the applicable Bulanov-Vasilyev-Frantsevich-Shevchenko system of equations of kinetics, has yielded a satisfactory correlation between experimental and actual service data covering temperatures from 343 K to above 3000 K. Materials with carbon-plastic reinforcement have been evaluated for the temperature dependence of its linear dimension during heating at various rates, also temperature and degree of reaction completion profiles across the ablation layer under the surface. In the case of glass-plastic reinforcement a set of five possible chemical reactions occurring each within a particular temperature range was considered: 1. $SiO_2 + C \rightarrow SiO + CO$, 2. $SiO_2 + 2C \rightarrow Si + 2CO$ 3. $SiO_2 + 3C \rightarrow SiC + 2CO$, 4. $SiO_2 + Si \rightarrow 2SiO$, 5. $Si + C \rightarrow SiC$. For materials with glass-plastic reinforcement have been evaluated: a. dependence of the loss of mass rate (kg/s) per unit surface area on the heat flow rate (kcal/s) per unit surface area, b. dependence of the thickness of the carbide layer on the ablation rate, c. dependence of the phase composition of the surface layer on the volume fraction of resin in it. It has also been determined how the pressure of phenolformaldehyde pyrolysis products within a cavity depends on the temperature inside it. The temperature range of mechanical tests was extended upwards by using specimens of a high-carbon matrix reinforced with tungsten fibers. For this composite material the temperature dependence of the bond strength at the interphase boundary has been evaluated. Figures 7; tables 4; references 32.

Ukraine: Accumulation of Solar Energy by Way of Thermochemical Transformations

964D0486G Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 7-8, Jul-Aug 95 pp 172-180

[Article by V.N. Bulanov and V.L. Klimenko, Institute of Problems in Materials Science at Ukrainian National Academy of Sciences; Kiev; UDC 661.96:661.931:537.22.662.997:662.93]

[FBIS Summary] Considering that endothermic chemical reactions effectively facilitate accumulation and storage of the heat of phase transitions, this concept is being applied to accumulation and storage of solar energy. A major drawback in this case is, however, inevitable dissipation of energy into space. Research done since the 1970s has established that most efficient such reactions are those which generate hydrogen. The combination of solar radiation and ever available water thus constitutes a not only inexhaustible renewable but also ecologically pure energy source. Concentrated solar radiation and thermochemical decomposition of water do also offer, especially during an "atomic pause", several techno-

logical advantages over other nonconventional primary energy sources. Thermochemical decomposition of water is essentially a multistage processes taking place in the presence of other reactants which, at the completion of this process, must have fully returned to their initial state. As such catalysts have been known S_2I_2, $CaBr_2$, and $FeCl_2$. More recently have been considered steam-to-gas conversion of methane $CH_4 + H_2 \rightarrow CO + 3H_2$ (possible at temperatures above 960 K) and dissociation of methane $CH_4 \rightarrow C + 2H_2$ (possible already at 850 K). Accumulation of solar energy is, by nature, not a continuous process so that ensuring a long-term repeatability of the process must be ensured and this requires ensuring adequate purity of all intermediate products of the thermochemical hydrogen generating reaction, which thus becomes still more costly than conventional electrolysis of water. Three types of methane conversion reactors have been designed for this application and thoroughly tested for a comparative performance evaluation: 1. a conical spiral reactor-collector, 2. a reactor with box-like cavities, 3. a cast reactor. The drawbacks of the first reactor were found to be high drag, underutilization of solar collector surface, and a large ratio of total reaction chamber surface to catalytic cavity volume. The second reactor, though free of these drawbacks, was not very efficient. The third reactor was the best, but it also performed below the theoretically possible. Later, throughout the 1980s, research and development work was done on thermochemical conversion of other hydrocarbons and coal, its feasibility being geographically limited. Lately being considered is generation of hydrogen by oxidation of iron (or lower-valence iron oxides by water vapor $Fe + H_2 \rightarrow FeO + H_2$ and by reduction of iron oxide by carbon monoxide $FeO + CO \rightarrow Fe + CO_2$. Other recent developments include gasification of solid fuels containing considerable volatile matter, costing less, and yielding a more hydrogen-rich gas mixture. An excellent such fuel is glass-textolite, which contains 30-50% polymer binder with a 10-40% coke number. Figures 1; tables 3; references 41.

Ukraine: Mechanism of Sintering Diamond Polycrystals Impregnated With Hard Alloy

964D0580A Kiev SVERKHTVERDYYE MATERIALY in Russian No 5, Sep-Oct 95 pp 3-7

[Article by L.F. Stasyuk, Institute of Superhard Materials imeni V.N. Bakuli at Ukrainian National Academy of Sciences, Kiev; (manuscript received 20 Jan 94) UDC 621.921]

[FBIS Summary] Polycrystalline tool materials containing diamond include composites ones consisting of diamond and a hard alloy. Plates of these materials are General Electric produces ("stratapax" and "compax") by by sintering diamond micropowders on hard-alloy substrates under a 6.0 GPa high pressure in a "belt" chamber at a 1500-1600°C temperature. It is being proposed to produce them by impregnation of the polycrystalline diamond layer with cobalt or by sintering diamond-cobalt mixtures. The author has made a thorough study of this sintering after impregnation process, for the experimental part of which plates were produced from grade ASM 60/40 synthetic diamond and W-Co 15 alloy. Sintering was done in a "toroid" high-pressure chamber under a 7.7 GPa pressure at 1500-2000°C temperatures and followed by isothermal soaking for 15-25 s. The author tentatively subdivides this process of sintering polycrystalline diamond into three successive stages: 1. raising the pressure in the chamber to 7.7 GPa with the action space remaining at room temperature (porosity of the diamond cake dropping from 45% to 19% and the diamond layer shrinking by the mechanism of brittle fragmentation) - 2. heating the action space to the hard-alloy melting point within 10-15 s (diamond layer shrinking by the mechanism of plastic flow and its porosity dropping to about 10%) - 3. impregnation of the diamond layer with the hard-alloy melt (final plate structure formed within 20-25 s of isothermal soaking). X-ray spectrum micoanalysis has revealed that the binder phase of this composite material contains 65-70 wt.% Co and 30-35 wt% W, which approximately corresponds to the composition of the Co-WC eutectic. No graphitization of diamond in the pores of the diamond compact was recorded during heating to the sintering temperature, but was recorded during sintering at temperatures higher than 2000°C. Figures 2; references 12.

Ukraine: Effect of Sintering Conditions on Optical Properties of Diamond-Like Carbon Films

964D0580B Kiev SVERKHTVERDYYE MATERIALY in Russian No 5, Sep-Oct 95 pp 11-16

[Article by V.A. Semenovich, N.I. Klyuy, S.I. Frolov, and V.A. Mitus, Institute of Superhard Materials imeni V.N. Bakuli and Institute of Semiconductor Physics at Ukrainian National Academy of Sciences, Kiev; (manuscript received 14 Oct 94) UDC 539.216.2:535.3]

[FBIS Summary] An experimental study of amorphous diamond-like carbon films was made concerning their optical properties and thus their suitability for use as transparent coatings on semiconductor layers. Such films were deposited, 100-1000 Angstroms thick, on quartz as well as Si and Ge substrates from the plasma of CH_4+H_2 mixtures in capacitive high-frequency (13.56 MHz) low-pressure (0.1-0.8 torr) electric discharge at room temperature (300 K), the volume fraction of methane in the mixture being varied from 10% to

30%. The rate of a-C:H film deposition was found to increase when either the high-frequency bias voltage at the substrate or the pressure within the reaction zone were raised, but to decrease when the $CH_4:H_2$ volume ratio was increased. More hydrogen in the mixture thus evidently intensified the process of methane dissociation and lowered the concentration of heavier hydrocarbon radicals, possibly by stimulating successive reactions in the gaseous phase and in this way converting those radicals into stable heavier hydrocarbon molecules. Under "mild" conditions, with the discharge voltage not exceeding 1000 V, the process yielded soft carbon films (hardness H approximately equals 0.6 GPa) with a rather high hydrogen content (up to 50 atom.%), and an approximately 3.3 eV wide forbidden band. With a higher discharge voltage and a lower methane content in the mixture were produced hard carbon films (H approximately equals 10 GPa) containing much less hydrogen (about 20 atom.%), having an only approximately 2 eV wide forbidden band, and featuring a high thermal stability. All films were tested in a spectral photometric ellipsometer with a rotating analyzer and in a laser ellipsometer for measurement of their refractive index and absorptivity over the 1.5-6.0 eV range of photon energy. The measurements have revealed how differently both optical properties of soft films and hard films depend differently on the high-frequency discharge voltage and on the photon energy of incident light. Measurements of their transmission coefficient in the infrared region of the spectrum (2.0-2.5 μm wavelengths) have also a revealed a large difference. Figures 5; references 11.

Ukraine: Kinetic Characteristics of Sphaleritic Boron Nitride Crystallization Process in BN-Li_3N-(H,N) System

964D0580C Kiev SVERKHTVERDYYE MATERIALY in Russian No 5, Sep-Oct 95 pp 16-21

[Article by V.B. Shipilo, L.M. Gameza, and A.I. Lukomskiy, Institute of Solid-State and Semiconductor Physics at Belarusian Academy of Sciences; (manuscript received 26 Apr 94) UDC 666.233]

[FBIS Summary] An experimental study of sphaleritic boron nitride BN_{sp} crystallization in the BN-Li_3N-(H,N) system was made concerning the kinetics of this process under six different sets of conditions: under two high pressures (4.2 GPa, 4.4 GPa) and at three different temperatures (1700 K, 1790 K, 1870 K) under each pressure. As the the initial graphitic phase BN_{gr} to be transformed into the sphaleritic one were used crystals of boron nitride with a G= 1.45 degree of graphitization, a= 0.2504 nm and b= 0.6658 nm lattice parameters, and a p_1= 0.85 degree of three-dimensional ordering. As the (H,N) impurity were added hydrogen or nitrogen compounds. The process was monitored over a 600 s long period and after its completion under each set of conditions, sphaleritic crystals were extracted from the cakes by treatment with acids and KOH melt. They were then rinsed with water, dried, and weighed before being passed through standard sieves for segregation into size fractions. The number of crystals (crystallization centers) in each fraction were counted under two microscopes: MBS-9 biological stereoscopic and MIM-8M metallographic. Two parameters characterizing the $BN_{gr} \rightarrow BN_{sp}$ transformation kinetics were calculated for the purpose of a comparative quantitative analysis: the transformation ratio $\alpha = m_{sp}\rho_{sp}/m_{gr}\rho_{gr}$ and the transformation rate $C = \Delta\alpha/\Delta t$ (m- mass, ρ- density, t- time). Under the 4.2 GPa pressure the transformation ratio was found to have been increasing monotonically (at a fast increasing rate during the initial incubation stage, at an almost constant rate during the smooth transition stage, at a slowly increasing rate before saturation) to α_{sp}= 0.22, 0.26, 0.30 at 1700 K, 1790 K, 1870 K respectively. The transformation rate under this pressure has been peaking to a maximum within some time after beginning of the process, reaching a higher maximum sooner at a higher temperature: C_{sp}= $14x10^{-4}$ s^{-1} in 165 s at 1700 K, C_{sp}= $15.5x10^{-4}$ s^{-1} in 135 s at 1790 K, C_{sp}= $16.7x10^{-4}$ s^{-1} in 105 s at 1870 K. Under the 4.4 GPa pressure the transformation ratio was found to have been increasing at a slowly decreasing rate from zero at the beginning of a now shorter incubation stage to a saturation level: α_{sp}= 0.24, 0.28, 0.32 at 1700 K, 1790 K, 1870 K respectively after 600 s. Under this pressure the transformation rate, initially high (C= $15.7x10^{-4}$ s^{-1} at 1700 K, C= $22.8x10^{-4}$ s^{-1} at 1790 K, C= $26.6x10^{-4}$ at 1870 K), was at each temperature first fast and then more slowly decreasing to a near zero saturation level after 600 s. In addition were also evaluated the kinetic characteristics of crystal nucleation and growth at each temperature under both pressures. The compressive strength of thus produced 160/125 grain-size BN_{sp} powder was within the 14-16 N range. Figures 6; references 5.

Kiev: Structural Changes Induced in Surface of Hard TiC and WC Alloys With Ni Binder by Laser Radiation

964D0597A Kiev POROSHKOVAYA METALLURGIYA in Russian Nos 9-10, Sep-Oct 95 pp 67-71

[Article by M.S. Kovalenko, A.V. Paustovskiy, V.N. Minakov, B.M. Boleyko, N.A. Yurchuk, and V.A. Tsyban, Institute of Problems in Materials Sciences

at Ukrainian National Academy of Sciences, Kiev; (manuscript received 6 Apr 87) UDC 621.762]

[FBIS Summary] The experimental study was made to determine the feasibility of modifying the surface structure of hard carbide alloys with nickel binder by laser treatment. Specimens of the TiC+(Ni-Cr) 70 alloy were produced by conventional pressing and sintering of compacts under vacuum. Their flexural strength was within the 1.1-1.4 GPa range, with grains in the 1.5-3.0 μm size fraction. Specimens of the W+Ni15 alloy containing WC carbide binder were produced by high-speed pressing of hot ingots, the advantages of this method over conventional sintering being its somewhat lower temperature and application of high pressure for a very short time (milliseconds) only. The impact strength of these specimens, with grains in the 1.2-1.3 μm size fraction, was 2.0-2.5 times higher than that of the conventionally produced alloy. All specimens were treated with laser pulses of 1 ms duration in an argon atmosphere, their energy being varied over the 1-25 J range. The original surface layers and the defective post-treatment surface layers were examined by metallographic methods under a Jeol-C T-20 scanning electron microscope, their phase composition was analyzed in a DRON-3.0 x-ray diffractometer, and their microhardness was measured in a PMT-3 tester with a 1.47 N indenter. The results have revealed a strong local effect of laser radiation. Its power density in this experiment was raised up to 600 J/cm². Raising it to about 300 J/cm² had caused the heat-affected zone to extend deeper and the microhardness to increase. Raising it further, 300-400 J/cm², had caused the heat-affected zone to continue extending deeper; in the TiC+(Ni-Cr) specimens with an attendant formation of craters due to cracking and evaporation, in the W+Ni15 specimens with an attendant formation of new phases (W_2C semicarbide and α-$WC_{hex} \rightarrow \beta$-$WC_{cub}$ transformation). Raising the radiation power density still higher did not further deepen the heat-affected zone in any specimen but increasingly degraded the properties of the surface layer material and led ultimately to its breakdown. Figures 4; tables 1; references 8.

Kiev: Effect of Heat Treatment on Microstructure, Strength, and Corrosion Resistance of Extruded Hard Alloy TiC

964D0597B Kiev POROSHKOVAYA METALLURGIYA in Russian
Nos 9-10, Sep-Oct 95 pp 71-75

[Article by V.A. Vlasov, T.N. Shishkina, G.N. Komratov, and A.V. Bokov, Institute of Structural Macrokinetics at Russian Academy of Sciences, Chernogolovka; (manuscript received 16 Sep 93) UDC 621.762.8:536.46]

[FBIS Summary] An experimental study was made to determine the effect of high-temperature annealing on the microstructure as well as on the strength and the corrosion resistance of the grade STIM-2 extruded Ti-C-Ni alloy used as electrode or tool material for various metallurgical processes (electric-spark alloying, hard facing). Test specimens were prepared from a mixture of 35 wt.% titanium powder + 35 wt.% carbon powder + 30 wt.% nickel powder which had been ground in a ball mill for 24 hours and then compacted into pellets under a pressure of 100 MPa for subsequent self-propagating high-temperature synthesis. Long cylindrical (2 mm in diameter) electrodes were then produced by hot extrusion of the plasic mass. They were then annealed at temperatures covering the 300-1200°C range for lengthy periods of time, oxidation being minimized by maintaining a high vacuum of 1 mPa throughout the process. Before and after that treatment they were tested for strength in bending and corrosion resistance, microstructural examination being included. The effect of this heat treatment at each temperature on their strength was evaluated in terms of the ratio $K = \sigma_{av.a}/\sigma_{av.b}$ (av.a- average before treatment; av.b- average after treatment). Vacuum annealing at 300-500°C and at 1000-1200° was found to have increased the strength, but not so vacuum annealing at 500-1000°C. Microstructural examination was performed in an "Epikvant" instrument, also before extrusion, to monitor changes of the TiC grain size distribution pattern depending on the annealing temperature. The grain size histograms indicate that high-temperature synthesis produced a material with grains covering the 2-25 μm size range, 2-3 μm being the largest fraction. Extrusion widened the size range slightly, making the 3-7 μm fraction the largest of all. Annealing at 800-950°C widened the size range further to 30 μmm. Annealing at 800°C increased the fractions of larger grains and annealing at 850°C increased their fractions maximally, but never making them exceed the fraction of small

grains. Annealing at 900-950°C decreased their fractions appreciably and annealing at 1000° narrowed the grain size range to 12 μm. Annealing at 1050-1300°C widened the size range: annealing at 1300°C made it 2-25 μm wide as originally. Electrodes for the corrosion test were soaked in nitric acid at room temperature for several days and periodically weighed. The results indicate that the solubility of this alloy may have been increased by annealing at 320-420°C, the α-Ni → β-Ni transformation range, was decreased by annealing at 450-1200°C. The fraction of undissolved material was over 60% after annealing at 500-600°C, while only 35-60% remained after annealing at 600-1200°C. The authors thank the staff of the plastic deformation laboratory headed by A.M. Stolin for supplying the electrodes, also A.M. Stolin and V.V. Podlesov for helpful discussion and suggestions. Figures 4; references 2.

Russia: Role of Dissolution Kinetics of Intermetallic Compounds During Al-Ti Alloying in Al Melts

964D0782A Yekaterinburg RASPLAVY in Russian No 6, Nov-Dec 95 pp 23-31

[Article by I.V. Polenta, I.G. Brodova, D.V. Bashlykov, A.G. Gudov, and T.I. Yablonskikh, Institute of Metal Physics at Russian Academy's of Sciences Ural Department, Yekaterinburg; (manuscript received 7 Feb 96)
UDC 669.715:669.046.516.4]

[FBIS Summary] An experimental study of Al-Ti alloys with a hardener was made concerning the dependence of their crystallization parameters on the method of hardener casting and the temperature-time conditions of its subsequent heat treatment. Melts of the commercial alloy AK6 (Al-2 Cu-1 Si-0.6 Mg-0.6 Mn) were alloyed with up to 0.15 wt.% Ti, this process taking place at a 990 K temperature with the Al-3.8% Ti alloy selected as hardener. The latter had been produced in three different ways: 1. by casting into heavy (5-7 kg) pigs according to factory procedure ("factory" hardener); 2. by casting the melt of FH hardener, overheated to 1650 K, into crucibles in air and thus forming light-weight (30 g) pebbles ("overheat" hardener); 3. by cooling the melt of "factory hardener", overheated to 1450 K, on a fast rotating copper cone and thus forming thin (100-500 gmm) fibers ("high-speed" hardener). The overheating temperature-time conditions were set so as to ensure homogenization of the melt, in the case of "high-speed" hardener also so as to achieve the desired solid-state structure. Batches of the AK6 alloy were placed in alundum crucibles and overheated to 990 K, wherepon hardener was added in an amount sufficient for a 0.15 wt.% content in the final product. After a 15 minute long mixing operation at that temperature, the melt was poured into chill molds. The ingots were then heat treated by quenching from 790 K and subsequent 3 h long annealing at 450 K. The microhardness of the castings was measured in a PMT-3 tester with a 20 g load, whereupon they were also tested for tensile strength. Metallographic examination was performed with a Neophot-2 reflecting microscope and a video camera connected to an IBM PC/AT computer for data processing with the ANALISER Standard Quantitative Analysis program package, the random error being minimized by raising the number of readings taken to several orders magnitude and by excluding the subjectivity factor. Structural examination was performed by the x-ray diffraction method. A special object of this study were inclusions, i.e., intermetallic compounds. In the "factory" hardener were found inclusions of primary Al_3Ti with a DO_{22}-type tetragonal crystal lattice, the distribution of these 250-300 μm large inclusions being extremely nonuniform. In the "overheat" hardener were found Al_3Ti inclusions of the same 250-300 μm size fraction and with the same DO_{22}-type crystal lattice, but the latter distorted by subboundaries and microcracks. In the "high-speed" hardener were found Al_3Ti inclusions with an ordered cubic L2-type crystal lattice, the distribution of these 3-5 μm large inclusions being uniform.

The results of this study indicate that the structurization of the alloy with hardener depends on the method by which the hardener has been produced. An explanation for the presence or absence of primary Al_3Ti in the alloy+hardener phase is sought in the peculiarities of isothermal dissolution of solid particles in a melt. For a theoretical analysis, this process is treated as a sequence of two phenomena: migration of atoms from the solid phase into the liquid one through the interphase boundary, followed by redistribution of these atoms in the liquid phase. Depending on whether migration or redistribution of the atoms governs the overall dissolution rate, the entire process is being characterized as a kinetic or diffusional one. The answer to what happens at the interphase boundary is sought by generalizing the Stefan problem in a spherical system of coordinates and solving it for the appropriate boundary constraints. A numerical analysis of the solution for Al_3Ti particles, aided by empirical and earlier experimental data, reveals how the time taken for Al_3Ti to dissolve in each of the two modes depends on both the initial size of Al_3Ti particles and on the temperature of AK6 melt. The results of this analysis, when correlated with the conditions of this experimental study, do quite adequately explain its findings. Figures 4; tables 2; references 13.

Ukraine: State Concept of Chernobyl Restricted Zone

964D0676 Kiev KONTSEPTSIYA CHORNOBYLSKOY ZONY VIDCHUZHENNYA NA TERYTORIYI UKRAYINY in Ukrainian 21 Feb 95 pp 2-24

["Concept" statement on the Chernobyl restricted zone of the Ministry for the Protection of the Population From the Aftermath of Chernobyl, signed 13 April 95]

[FBIS Translated Text] Ministry for the Protection of the Population From the Aftermath of Chernobyl

Concept of Chernobyl Restricted Zone

The approved portion:

In accordance with the Cabinet of Ministers of Ukraine assignment No. 3549/97 of 21 February 1995, the "Concept" has been approved at the Ministry for the Protection of the Population From the Aftermath of Chernobyl board meeting 13 April 95.

[Signed] V.I. Kholosha, acting minister [signed] A.P. Sokolov, director, Kiev "Energoproekt" Institute [signed] E.V. Sobotovych, science leader, academician, Academy of Sciences of Ukraine Kiev, 1995

Principal authors:

Sobotovych, E.V. — VRNS IGMR, Academy of Sciences of Ukraine

Kholosha, V.I. — Minchornobyl Ukrayiny

Skvortsov, V.V. — VRNS IGMR, Academy of Sciences of Ukraine

Okhovyk, Yu.O. — Same

Olshtynskyy, S.P. — Same

Zaytsev, Yu.P. — ISPE, Academy of Sciences of Ukraine

Prantsevych, L.I. — IZ, Academy of Sciences of Ukraine

Davydchuk, V.S. — IG, Academy of Sciences of Ukraine

Shestopalov, V.M. — Scientific Research Center, RPD, Academy of Sciences of Ukraine

Popova, L.M. — Inter-Branch S&T Center, Chernobyl Institute, Academy of Sciences of Ukraine

Okhevskiy, V.G. — RAVS, Academy of Sciences of Ukraine

Koval, G.M. — IYaD, Academy of Sciences of Ukraine

Kupryy, V.I. — AZV, Minchornobyl Ukrayiny

Proskura, M.I. — Same

Krymka, L.A. — IYaD, Academy of Sciences of Ukraine

Bobylyova, O.O. — Ministry of Health of Ukraine

Voytsekhovych, O.V. — Minchornobyl Ukrayiny

Nasvit, O.I. — Same

Loshchylov, M.O. (deceased) — UkrNDISGR

Bitskyy, A.A. — MNTs "Shelter," Academy of Sciences of Ukraine

Yakovlev, I.O. — State Committee of Ukraine of Geology and Utilization of Mineral Wealth

Leytsyn, V.M. — Kiev Institute "Energoproekt"

Rozanov, D.V. — Same

Contents

Introduction

The Chernobyl Restricted Zone (hereafter "the Zone") is the territory of Ukraine contaminated with radionuclides as a result of the Chernobyl catastrophe. Its land has been taken out of the national economic rotation, with a special form of management performed by the Zone Administration. Per Law of Ukraine "On the Legal Status of the Territory That Sustained Radioactive Contamination as a Result of the Chernobyl Catastrophe" the Zone is defined as the territory from which the population was evacuated in 1986. The Zone area is 2,044 km². Within it there are two towns (Pripyat and Chernobyl) and 74 villages, including seven villages outside the main territory.

Radioactive contamination of the Zone as a result of possible escape of radioactive substances beyond its boundaries constitutes a certain hazard for Ukraine which is due to its strategic geographic position in the supply basin of Ukraine's main water artery, the river of Dnieper.

Current Status of and Activities Inside Restricted Zone

The main sources of ionizing radiation are as follows:

Radioactive Contamination of the Environment. The distribution of radioactive contamination over the Zone territory is not uniform in terms of contamination density, radionuclide composition and the ratio of various forms of radioactive fallout and is represented mainly by radionuclides of cesium-137, strontium-90 and transuranium elements. As of 1 January 1994, about 95 percent of radioactive contamination was concentrated in the top 5-cm soil layer.

Surface radioactive contamination of the Zone territory (without taking into account areas of localization of radioactive waste (RAW) and ChAES [Chernobyl AES] industrial site) is 110 thousand Qi of cesium-137, 127 Qi of strontium-90 and 800 Qi of plutonium-239-240. The territory with the contamination level above 15 Qi/km² of radiocesium, 3 Qi/km² of radiostrontium and 0.1 Qi/km² of plutonium covers 1,856 km².

"Shelter" Facility. According to maximum estimates, in the "Shelter" facility there are approximately 180 metric tons of nuclear fuel which contains radioactive substances with an over 20 million Qi activity. In addition to fuel-containing masses (FCMs) the "Shelter" facility contains a large amount of radioactive waste consisting of remnants of the core of the destroyed reactor, reactor graphite and contaminated metal and construction structures of the power unit.

ChAES Spent Nuclear Fuel (SNF) and Radioactive Waste. As of 1 January 1993, there were 13,300 spent fuel assemblies in the ChAES spent nuclear fuel repository (SNFR). The volume of waste accumulated at the ChAES is estimated as follows: 33,800 m³ of solid RAW (SRW) and approximately 30,000 m³ of liquid RAW (LRW); as a result of ChAES activity 2000 m³ of SRW and 870 m³ of LRW are generated annually.

RAW Burial and Temporary Localization Sites. In the three radioactive waste burial sites (RWBSs) and temporary radioactive waste localization sites (RWTLSs) that were organized during the emergency and decontamination operations there are radioactive materials with the total activity that as of 1 January 1990, was estimated at 380,000 Qi, with the total volume of approximately 1 million m³.

The Zone RWTLSs are a conglomeration of over 800 structurally simple buildings.

The ChAES cooling pond is a water reservoir with a 22.9 km² area; it holds 160 million m³ of water. In 1989-1993 average annual water contamination in the cooling pond varied between 140 and 330 pQi/l of cesium-137 and between 120 and 330 pQi/l of strontium-90. The overall radionuclide activity in bottom sediments was reaching as high as 3,500 Qi of cesium-137, 800 Qi of strontium-90 and 3 Qi of plutonium 238-239.

Radionuclide Migration Beyond Zone Boundaries. The main routes of radionuclide migration beyond the Zone boundaries are annual runoff (formed due to surface runoff and removal of radionuclides by groundwater), air (wind) transport, biogenic transport, and technogenic transport.

The main rout of radionuclide migration beyond the Zone boundaries is surface runoff. In 1989-1993 the average annual radionuclide runoff from the river of Pripyat into the Kiev water reservoir was 112-426 Qi of strontium-90 a year (including approximately 60 percent from the Zone) and 52-125 Qi of cesium-137 (not more than 20 percent from the Zone).

Air (wind) transport of radionuclides plays a negligible role compared to water transport. Dense vegetation cover in fallows and forests almost completely prevents wind transport (one is not taking into account escape of radioactive substances during fires).

Biogenic transport of radioactive contamination beyond the Zone boundaries does not exceed several Qi/year of cesium-137 and strontium-90.

According to approximate estimates, technogenic migration of radionuclides beyond the Zone boundaries is less than 1 Qi a year. As of 1 January 1994, radionuclide migration into groundwater had not caused stable area contamination of groundwater over a large part of the Zone territory. Radionuclide accession into groundwater is the most intensive in the areas where RWTLSs are located, where 0.03-3 mcQi/l concentrations of strontium-90 in groundwater are observed. The process of radionuclide migration from the ground surface is fairly protracted over time, so the maximum content of strontium-90 in groundwater is expected 20-30 years after the Chernobyl catastrophe.

At present the Zone contribution to the collective radiation dose of Ukrainian population via all radionuclide migration routes does not exceed one percent.

Condition of Land and Forests. The radiation effect caused destruction of biocenoses over the area covering not more than 0.3 percent of the Zone territory.

Over 2 to 3 percent of territory activity is conducted within the boundaries of towns and industrial zones. In the remaining 97 percent of the Zone territory the change of biocenoses is determined by cessation of human activity rather than by radionuclide contamination.

Activity in Zone

Production activity in the Zone is conducted along two directions: operation of the Chernobyl AES and performance of work aimed at minimizing the aftermath of the Chernobyl catastrophe and at Zone maintenance. The activity is conducted by five main organizations - production association "ChAES", scientific production association "Pripyat", construction administration "ChAES", interbranch S&T center "Shelter" of the National Academy of Sciences of Ukraine and specialized state integrated production enterprise "Chornobyllis".

In addition, over 120 scientific research, production, design and planning, start-up and debugging, and repair organizations and enterprises work in the Zone. It is necessary to better coordinate the activity of the enterprises and organizations related to eliminating the consequences of the Chernobyl catastrophe. Twenty-three facilities are functioning in the areas of medical, commercial, communal and transportation services, public catering, fire protection, communications, daily life and leisure.

As of 1 January 1994, the total number of workers in the Zone was about 15,000, including the ChAES personnel.

No agricultural activity aimed at producing marketable products is conducted in the Zone.

Organization of manufacturing activity in the Zone provides for adhering to principles of radiation safety and medical control of the personnel. Medical-sanitary and dosimetric support of the personnel is provided by specialized subdivisions and services.

The current infrastructure of the Zone does not fully meet production and social goals.

1. General Provisions of Concept

The concept of the Chernobyl Restricted Zone in the territory of Ukraine and activity in the Zone (hereafter "the Concept") has been developed for the period up to 2020-2025. Because of the complex character of problems and possible changes in current legislative and other normative documents and adoption of new legislative acts the Concept shall be clarified and corrected periodically (at least once every five years).

1.1. Purpose and Objective

Based on current normative and legislative documents the Concept defines the system of organizational, environmental, medical and S&T principles and priorities of production and S&T activity in the Zone aimed at minimizing environmental and sociopolitical consequences of the Chernobyl catastrophe.

The Concept objective is to determine ways for long-term maintenance of the Zone and activity priorities there along main directions that ensure reduced environmental risk level and minimize the Zone impact on the radioenvironmental situation in Ukraine.

1.2. Legal and Regulatory Basis

The Concept is based on Laws of Ukraine "On the Legal Regime of the Territory That Sustained Radioactive Contamination As a Result of the Chernobyl Catastrophe" and "On the Status and Social Protection of Citizens That Have Suffered As a Result of the Chernobyl Catastrophe", as well as on legislative and normative acts (Appendix).

The natural resources of the Zone are the exclusive property of the people of Ukraine. Real estate objects located in the Zone are the property of the state; no change of their forms of ownership is anticipated.

1.3. Scientific Basis of Concept

The Concept is based on results of generalization of factual information and conclusions of scientific research work related to studies of the status of objects containing radioactive materials and of the Zone environment, including forecasts of probable environmental consequences of the Chernobyl catastrophe, in particular:

— on conclusions about a relative stability of the radioenvironmental situation in the Zone and in rivers and water reservoirs of the Dnieper cascade that are connected to the Zone;

— on the existence of real technical ability to convert objects containing radioactive materials into environmentally safe systems and transform materials localized in them to a condition that prevents radionuclide accession into the biosphere.

1.4. Concept Implementation Stages

The full implementation of Concept objectives cannot be achieved within a short time frame. Their actual implementation, taking into account activity priorities in the Zone, depends on technical and economic resources. The Concept is being implemented in two stages.

The first stage is implementation of measures stipulated in the National Program of Eliminating the Consequences of the Chernobyl Catastrophe and Socioeconomic Protection of Citizens, development of criteria for dividing the Zone territory into districts, and preparing a feasibility study (FS) of the immediate measures that must be implemented within the next two to four years.

The second stage is the implementation of measures developed during the first stage, preparation of FS and development of projects of further measures that must be implemented within eight to ten years, and fulfillment of long-term measures aimed at implementation of the main objective of the Concept.

2. Functional Division of Zone Territory Into Districts

To conduct the activity aimed at transforming the Zone into an environmentally safe system it is necessary to divide its territory into districts according to prevailing types of activity in various parts of the Zone, to prospects of returning the land to the national economic rotation and to the value of environmental systems. The division into districts is done in order to preserve the natural wealth of the Zone and ensure its reasonable utilization in the future taking into account the following:

— the disproportionate character of radioactive contamination of the terrain;

— the location of RWTLSs and RWBSs;

— the location of operating enterprises and infrastructure elements;

— the location of the planned complex for RAW processing and localization;

— the variety of the natural conditions in the Zone;

— the need to preserve existing natural preserves;

— forecasts of changes in the environmental status of the Zone.

It is expedient to divide the Restricted Zone into four functional parts: industrial, guarded (buffer), preserve and general regime zones. For each zone a special regime is instituted that regulates the types of personnel activity, and the size and length of their stay.

2.1. Industrial Zone

The industrial zone where the main work related to elimination of the consequences of the Chernobyl catastrophe is performed consists of two parts that differ in the density and composition of radionuclide contamination and in the character of activity:

— a conditionally "dirty" zone—the territory where work is performed to convert the "Shelter" facility to a safe state, to process and store RAW, to operate and decommission the ChAES and to protect the river of Pripyat floodplain from submersion during floods, and where sanitary and fire protection measures in forests are implemented;

— a conditionally "clean" zone—the territory where the elements of production activity and the Zone infrastructure that supports production activity are concentrated.

In these territories it is planned to implement different regulations for labor safety and radiation protection of the personnel. A special sanitary-access regime is being implemented in the conditionally "dirty" zone. The territory of the industrial zone covers 80-100 square kilometers.

2.2. Guarded (Buffer) Zone

The guarded (buffer) zone is the territory with low density of radioactive contamination and with the prospect of being returned to the national economic rotation for agricultural use within the next several decades.

This zone is characterized by restriction of activity in accordance with the main principles of the Concept. Within its boundaries it is planned to implement forest

restoration measures taking into account the prospect of returning the territory to the national economic rotation.

Certain areas can be used as scientific research, etc. test grounds.

2.3. Preserve Zone

The preserve zone covers at least 10 percent of land and forests. Within this territory of the Zone a preserve regime is maintained which prevents disturbance of the natural course of self-restoration of ecosystems by limiting the length of personnel stay in accordance with the preserve status.

2.4. General Regime Zone

The general regime zone covers the rest of the Chernobyl Restricted Zone except the above listed territories. As far as its status is concerned this is a preserve where it is necessary to perform forest restoration work, scientific research and work aimed at maintaining the Zone regime and preservation of cultural values.

2.5. Zone Boundaries

The outer boundaries of the Zone are defined by normative acts. The Zone boundaries can be changed taking into account the Concept requirements to population residence in Ukraine territories with increased levels of radioactive contamination caused by the Chernobyl catastrophe, based on medical and other criteria of population residence in environmentally dangerous regions, after the criteria are clarified and approved according to the established order.

The territory that is being removed from the Zone in order to be returned to the national economic rotation is excluded from the authority of the Zone Administration according to the established order and is not covered by Concept provisions thereafter.

3. Activity in Zone: General Provisions

3.1. Objective of Activity in Zone and Goals of Eliminating Consequences of Chernobyl Catastrophe

The main objective of the activity in the Zone aimed at eliminating the consequences of the Chernobyl catastrophe (hereafter "the activity"; the Chernobyl AES operation will be mentioned separately) is to minimize the environmental hazard of the Zone and in perspective to convert it to a state that is environmentally safe for Ukraine population at all stages of the Zone maintenance.

This objective determines priorities of investing money and labor and material resources in any activity in the Zone territory.

The main directions of the activity in the Zone are as follows:

— protecting Ukraine population from radiation exposure the sources of which are located in the Zone, and radiation protection of the personnel working in the Zone;

— converting technogenic facilities containing radioactive materials to a controlled state;

— landscape restoration aimed at limiting radionuclide migration and reducing the environmental effect of radioactive contamination;

— organizing monitoring of Zone environment;

— conducting scientific research;

— preserving historical and cultural landmarks;

— providing the infrastructure necessary for supporting the activity and stay in the Zone.

3.2. Basic Principles of Activity

The activity in the Zone shall be aimed at minimizing, as much as possible and economically justified, the environmental hazard of the Zone for Ukraine population taking into account extreme natural situations that are probable under the region's conditions.

In the Zone it is only permissible to perform work that does not worsen the radiological environmental situation and does not hinder reasonable utilization of the Zone territory in the future. The scope of radiation-hazardous work and the number of people working in the zone shall be as low as necessary.

Any activity in the Zone aimed at improving the radioenvironmental situation shall be performed with the maximum possible use of natural factors and minimal environmental interference that results in changing the direction of the natural processes of self-cleaning of the territory.

Based on current normative documents a radiation protection system shall take into account the specific conditions in the Zone. Radiation protection-related measures shall only be aimed at the Zone personnel (the Zone status includes residence of population in the Zone). Due to the presence of uncontrolled (dispersed) radiation sources, minimization of doses of external and internal radiation shall be ensured by a regime of strict restrictions and administrative control.

3.3. Production Activity in Zone

According to the Law of Ukraine "On the Legal Status of the Territory That Sustained Radioactive Contamination as a Result of the Chernobyl Catastrophe" it is

prohibited in the Zone to perform activity with the purpose of obtaining marketable goods without the special permission of Minchornobyl Ukrayiny.

The main types of activity are related to the following:

— ChAES operation;

— implementation of stages of ChAES decommissioning (construction of the necessary facilities and performance of the appropriate work is planned);

— converting the "Shelter" facility into an environmentally safe system;

— creation of a complex of RAW processing and storage enterprises;

— implementation of forest and water protection measures; monitoring of the Zone environment;

— creation of the necessary infrastructure that would support activity in the Zone;

— implementation of other directions of production activity (including decontamination) that do not contradict the current Ukraine legislation and this Concept.

The activity of enterprises operating in the Zone is subject to insurance in accordance with current legislation.

4. Converting "Shelter" Facility Into Environmentally Safe System

Ways for implementation of this activity direction have been determined based on the international competition of projects and technological solutions related to converting the "Shelter" facility into an environmentally safe system and are presented in the "Concept of Converting the 'Shelter' Facility Into an Environmentally Safe System" developed by the jury of the competition.

Conversion of the "Shelter" facility into an environmentally safe system can be accomplished using either of the following alternatives:

— Removal of FCMs and other RAW from the facility to organized and managed storage;

— creation of a guaranteed safe system without removing FCMs and other RAW from the facility.

The main requirements for converting the "Shelter" facility are as follows:

— durability of the converted facility;

— control and adherence to the rules of nuclear, radiation, environmental and general technical safety at all stages of work related to converting the facility into a safe system and during subsequent operation in accordance with then-current normative documents;

— conversion work compatibility with ChAES operation, work on ChAES decommissioning and other directions of the necessary activity in the Zone.

5. ChAES Operation and Decommissioning

The Verkhovna Rada of Ukraine made a decision on continuing the term of ChAES operation. ChAES operating activity and its goals and objectives are determined by the State Program for Generation of Electric Power.

The terms of operating ChAES power units are determined by their technical condition and implementation of safety improvement measures and shall be established by agreement with regulatory bodies.

After stopping the ChAES it is planned to implement the Program "ChAES Decommissioning" developed in accordance with the "Concept of Decommissioning the Chernobyl AES" coordinated according to the established order.

According to the above documents the following is planned:

— converting the power units to a nuclear-safe state by performing the entire complex of work related to this stage that would ensure reliable operation of buildings and structures in the lay-up mode;

— unloading and storage nuclear fuel;

— long-term lay-up and aging of main buildings and components characterized by high level of contamination while at the same time performing dismantlement work at other buildings;

— performing main dismantling work after aging for 15 to 20 years.

6. RAW and SNF Treatment and Storage in Zone

An integrated solution of the RAW treatment problem requires one to solve the problem of building a RAW processing and localization complex based on using remotely controlled machines and mechanisms and robotic complexes.

RAW that has accumulated during ChAES operation and will be generated during ChAES decommissioning shall be processed using special equipment built at the ChAES, with RAW solidification, compaction and inclusion into matrices which will ensure their long-term storage and safekeeping.

SRW and LRW accumulated and generated as a result of activity in the Zone shall be processed and stored in accordance with current normative documents.

Environmental safety of existing RWBSs and RWTLSs shall be ensured by creating conditions for reliable long-term controlled RAW storage. In doing so the most important objectives are taking a complete and detailed inventory, environmental assessment of existing RWBSs and RWTLSs and making decisions to perform work on:

— Improving insulating properties of existing RWBSs, based on assessment and forecasting their condition;

— implementing measures ensuring reliable long-term storage of RAW in RWBSs and RWTLSs;

— RAW reburial.

The need to rebury RAW from RWTLSs can only be determined after performing the entire complex of research related to studying RAW hazards. When the question of the need to rebury is uncertain, the preference shall be given to scientifically substantiated methods for conservation of RAW in RWTLSs without opening them up.

The need to create additional surface-type repositories in the Zone territory for storing 1st and 2d group RAW shall be justified by results of assessing the environmental safety of existing RWBSs and RWTLSs, as well as taking into account characteristics of RAW to be processed.

The technology for treatment of 3d group RAW removed from the "Shelter" facility shall include waste separation into nuclear-hazardous (fuel-containing) and nuclear-safe waste with RAW conditioning, compacting and inclusion into stable matrices, containerization and transportation for storage.

The long half-life and high toxicity of radioactive substances contained in 3d group waste present requirements related to environmentally safe functioning of the waste burial system for several thousand years, which can only be ensured in geological type repositories. In terms of geological conditions the Zone territory is not suited for placing there such repository. It is therefore necessary to provide for creation of a temporary repository designed for long-term storage for up to 100 years with subsequent RAW reburial in a national repository.

Implementation of all measures related to RAW treatment and functioning of respective systems, including RAW storage, shall satisfy continuous long-term control requirements.

The issue of creating a National Center for Processing and Storage of 1st and 2d Group RAW requires special consideration at the state level according to the established order.

Measures related to long-term storage of SNF are implemented in two stages:

— first stage—transportation of spent nuclear fuel from cooling ponds of ChAES power units to the existing SNFR with subsequent storage;

— second—moving SNF to SNFR-2 for long-term storage.

It is necessary to build SNFR-2 is because conditions for storing SNF in the existing SNFR do not meet normative requirements.

The problem of further treatment of SNF must be solved within the framework of the National Program of RAW Treatment in Ukraine.

6.1. Processing and Storage in Zone of RAW stored at UDO special works "Radon" and of Industrial Waste

The feasibility of placing in the Zone production facilities for processing and storage of toxic and other industrial waste from settlements located in adjacent territories (including the city of Kiev) and RAW stored at the UDO special works "Radon" has not yet been determined unambiguously and calls for special analysis of all environmental aspects of the problem and development of appropriate technical and economic justification.

Processing and storage of industrial and household waste generated in the Zone in the process of personnel's activity are conducted in accordance with appropriate normative documents.

7. Long-Term Maintenance of Zone Territory

Long-term maintenance of the Zone territory is determined in accordance with basic principles of activity there and taking into account the following:

— low levels of radioactive contamination of certain Zone areas that do not exceed contamination levels of territories adjacent to the Zone;

— current formation, with the prospect of improvement, of a broad monitoring network that makes it possible to provide rapid response to possible negative processes in the Zone ecosystem that can result in increased radionuclide migration beyond its boundaries.

When necessary, activity in the Zone aimed at maintaining its territory shall be coordinated with the program of work performed in the territory of the State Woodland Radioenvironmental Preserve in Republic Belarus.

The strategy of treatment of environmental objects is built based on the functional division of the Zone territory.

7.1. Land and Forests

As a result of decontamination of the most contaminated areas of the Zone that had been conducted in 1986-1988, some radioactive materials that had entered the environment were localized. The experience demonstrates the inexpediency and insufficient efficiency of the accomplished measures as far as decontamination of land and forests is concerned. Therefore, it is not feasible to perform additional work aimed at decontamination of land and forests in order to improve the radioenvironmental situation in the Zone.

In the case of an unforeseen catastrophic deterioration of the radiation situation over limited areas the need for land and forest decontamination must be additionally justified.

The priority role belongs to the natural process of restoration of vegetation and animal communities with transition of ecosystems to a stable state that was typical for the region before the start of intensive human activity.

In order to stir up landscape restoration processes in the territory of the industrial and buffer zones and the general regime zone the following is planned:

— forest planting in floodplains with using attendantless technology of growing the plantations;

— non-interference into processes of overgrowing of land reclamation channels in order to renew the naturally determined level of groundwater;

— establishing mineralized fire protection strips while preserving natural tree saplings that would propagate from the forest wall.

It is prohibited to use land in the Zone for obtaining agricultural products.

Frontier areas of land and forests that, according to medical and other criteria, are suitable for returning to the national economic rotation with the purpose of agricultural use shall be removed from the Zone.

7.2. Zone Settlements

Surface radioactive contamination of the territory of non-operated Zone settlements, with housing and buildings located there, is no different from radioactive contamination of the adjacent terrain. It is therefore planned not to interfere in the processes of natural decay of housing and buildings in non-operated Zone settlements, except architectural, cultural and historic landmarks which shall be preserved. It is necessary to continue the work related to identifying them in the Zone territory.

The further fate of towns of Pripyat and Chernobyl-2 (deterioration, dismantlement or preservation for possible future use) shall be determined after performing additional studies including integrated analysis of proposed solutions.

7.3. Forests and Fire Protection Measures

The complex of forest preservation and fire protection measures in the entire Zone territory provides for creation of the following systems:

— control of the sanitary condition of the forests;

— man-made barriers in the form of gaps in existing forest cuttings and roads;

— mineralized fire protection strips that insulate forests from fallows beyond the boundaries of clearing zones where forest advance on fallows is the most intensive;

— fire protection inspection and special communications.

The following shall be accomplished:

— equipping fire and chemical protection stations with appropriate equipment;

— reconstruction of fire protection reservoirs;

— fire protection measures in non-operated Zone settlements.

Specialized enterprise "Chornobyllis" shall perform a complex of work on fallows forestation and forest restoration in burnout areas.

Forestry measures aimed at stabilizing the environmental situation shall be performed only by coordination with regulatory bodies.

Any lumber obtained as a result of sanitary deforestation and cleaning of forest cuttings shall be first of all used for internal needs of the Zone.

Removal of excess forest products from the Zone shall be performed in accordance with current legislation.

7.4. Water Protection Activity

The objectives of water protection activity are as follows:

— maintain in working order the currently operating water protection facilities (except the amelioration network);

— justify the need for additional (besides the current ones) water protection measures that could reduce radionuclide migration beyond the Zone boundaries and into the river of Dnieper, and choose priorities based on the cost-benefit analysis taking into account the input to the collective radiation dose of Ukraine's population from sources that are being localized;

— implement justified (in accordance with the above) additional water protection measures.

At an appropriate stage of work related to ChAES decommissioning the cooling pond shall be eliminated while implementing measures to prevent dust lifting of radionuclides from its bed.

The system of floodplain lakes that will remain after elimination of the cooling pond, together with lake Glyboke on the left bank of the river Pripyat will form test grounds for organizing scientific research.

7.5. Envirol Protection

It is planned to implement measures aimed at protecting natural landmarks and determining objects of the preservation zone.

The commissioning of new and operation of existing production capacity in the Zone shall be conducted in accordance with current normative acts that provide for implementation of environmental protection measures.

Exogenetic geological processes, flooding, overdrying and ground deformation that accompany landscape restoration shall not be corrected by man provided they do not result in increased release of radionuclides from the Zone and do not hinder normal enterprise activity.

7.6. Access Control Regime and Zone Protection

Protection and adherence to regimes in the Zone territory are enforced by special units of the Ministry of Internal Affairs and departmental militia.

The main objectives of the access control regime and Zone protection are as follows:

— prohibition of activity that contradicts laws of Ukraine, as well as activity that is not specified in documents that determine and regulate the directions and type of activity in the Zone;

— law enforcement;

— prohibition of technogenic propagation of radioactive contamination from the Zone territory to adjacent regions.

To achieve this, it is planned to:

— implement a complex of organizational and technical measures aimed at preventing unauthorized activity and penetration of unauthorized persons and vehicles into the Zone, control removal (bringing in) of material valuables and ensure law enforcement;

— complete construction of the perimeter fence;

— create a protective signaling system;

— build additional access control stations (ACSs) and install dosimetric control equipment.

Visits of the Zone by citizens are conducted based on specially developed programs approved by the Zone Administration and on following radiation safety standards and rules.

8. Socioeconomic Activity

In the sphere of socioeconomic activity it is planned to implement the following measures:

— convert the town of Chernobyl infrastructure and the entire Zone infrastructure in accordance with the objectives of long-term problem-oriented functioning of its production and scientific research complex;

— solve problems of socioeconomic development in settlements located in the vicinity of the Zone in correlation with prospective directions of Zone functioning;

— transfer persons that work in the Zone and live in the watch village (w/v) Zelenyy Mys to the town of Chernobyl because the design life of the w/v Zelenyy Mys housing is five years and the housing is unfit for continuous use;

— providing conditions for temporary dwelling of "squatters" in the Zone in accordance with current legislation and normative acts;

— cessation in the future of all kinds of production activity in the town of Pripyat and transferring all services and organizations from the town;

— development and implementation of an integrated program of additional measures for social protection of persons who work in or are being transferred from the Zone as a result of closing of enterprises and organizations or their subdivisions, as well as due to medical indications.

9. Medical and Sanitary-Hygienic Measures and Measures for Radiation Protection of Personnel

Because the Zone personnel works under the conditions of a serious radiological situation, which has mainly formed as a result of the presence of uncontrolled (dispersed) sources of ionizing radiation, it is necessary to conduct regular correction and reconstruction of the system of medical, hygienic, epidemiological and radiation control and corresponding radiation sanitary-hygienic and treatment and prophylactic measures, taking into account new scientific achievements, as well as social factors and political decisions.

To do this, it is necessary to amend departmental instructions while fully taking into account the specificity

of work performance in the Zone. The Zone Administration is charged with organizing the execution of instructions requirements.

Measures aimed at labor safety and radiation protection of the personnel shall include the following:

— organization of radiation control of the personnel, workstations, vehicles, housing and other facilities;

— strict adherence to medical requirements to the personnel including setting restrictions in terms of age, gender and medical contraindications;

— sticking to personal hygiene and mandatory use of individual protection and working clothes, preventive measures, and strict adherence to the sanitary access regime of the Zone;

— mandatory substantiation of the necessity and possibility of performing the work;

— strict restrictions on issuance of permits for planned additional exposure of the personnel; introduction of permissible and control levels;

— improving living conditions of the personnel in the Zone, including provision of a reliable heating, water supply and waste water disposal system, as well as reconstruction of sewage purification works; improving the sanitary and technical condition of public catering facilities and water supply sources including "squatter" housing; taking inventory and elimination of unorganized garbage dumps, and utilization of pesticides;

— mandatory sanitary-hygienic education;

— improving the medical service system and personnel including medical selection, outpatient supervision, strict adherence to treatment and prophylactic nutrition, etc.

10. Environmental Monitoring in Zone

The Zone monitoring system is being developed according to current normative acts. The program of developing a unified Zone monitoring system as a part of State monitoring of the environment shall be developed and implemented based on improving and combining the existing monitoring networks and methods.

The monitoring is conducted along the following main observation directions:

— radiochemical condition of landscapes and the air basin in order to assess and predict the general radioecological situation in the Zone and situations in its individual regions, as well as the environmental effect of the Zone on adjacent territories of Ukraine;

— concentration of radioactive substances in surface waters in order to assess and predict the effect of release of radionuclides on the environmental situation beyond the Zone boundaries;

— the state of the hydrogeological system in order to assess the hydrodynamic and radiochemical condition of groundwater and predict their effect on the environmental situation in the Zone and beyond its boundaries;

— exogenetic processes, flooding and overdrying of certain areas of the territory that accompany the process of landscape restoration;

— local sources of radionuclide contamination of the landscape-geochemical environment (RWBSs and RWTLSs);

— nuclear-radiation and radiogeochemical environmental effect of the "Shelter" facility;

— the radiation situation at the ChAES industrial site during its operation and at all stages of implementation of the ChAES decommissioning program;

— the radiation and radiogeochemical situation in the area of the proposed placement of the RAW processing and storage complex and its environmental effect at all stages of project implementation;

— the condition of biocenoses as factors and indicators of changes of environmental situations at all stages of implementation of Zone maintenance measures;

— the health status of the personnel and "squatters" and the sanitary-hygienic condition of the infrastructure at all stages of implementation of Zone maintenance measures.

Analysis and generalization of information on the condition of the Zone environment is conducted by the Administration (or an organization the Administration has authorized to perform this work).

Forecasting changes in the condition of the environment (or of its individual components) is done by the Administration with enlistment of scientific research institutions and creative collectives.

11. Management of Restricted Zone

The Zone management is performed by the Administration which is the state executive body in this territory.

The Administration organizes and coordinates all measures in the Restricted Zone territory, makes decisions on their financing, law enforcement and health of the personnel working in the territory, and protection of scientific and economic interests of the state; it is also

responsible for timely, comprehensive and objective information of Ukraine's population on the environmental situation in the Restricted Zone.

The functions of state supervision and regulation are performed by appropriate regulatory bodies of Ukraine within the limits of their authority.

Administration's decisions within the limits of its authority are mandatory for execution by all enterprises, institutions and organizations located or enlisted for work in the Zone, regardless of their agency subordination.

The main management functions of the Administration within the limits of its authority provide for the following:

— organization, financing and control of work related to eliminating the consequences of the Chernobyl catastrophe and long-term maintenance of the Zone stipulated by this Concept;

— organization, financing and control of work related to RAW treatment in the Zone;

— the function of control of adherence to the Zone regime;

— the permitting function in issues of conducting work (including new construction), creation, placement and closing of enterprises in the Zone;

— the supervisory function in issues of conformity of activity in the Zone to regulatory legal acts;

— the information function in all issues of activity in the Zone, analysis and generalization of information on the environmental condition in the Zone, liaison with the public, development and maintenance of the data bank on the work that is being and has been performed in the Zone;

— organization of performance of a complex of land regulation work in the Zone territory;

— organization of work on international cooperation in solving problems of eliminating the consequences of the Chernobyl catastrophe.

The Administration functions can be clarified taking into account the need to interact with controlling and regulatory bodies and in accordance with changes in Ukraine's legislation.

In order to define the required S&T and economic policy as to the activity in the zone, appropriate interagency S&T and production consultative bodies are organized under the auspices of the Administration.

12. Scientific Research in Restricted Zone

The Zone territory is a unique scientific research ground for studying the effect of radioactive contamination on the environment. Scientific research in the Zone shall be performed and coordinated within the framework of the National Program of Eliminating the Consequences of the Chernobyl Catastrophe. It is deemed possible to conduct scientific research work in the Zone within the frameworks of other programs if the need and feasibility of conducting them in the Zone territory are justified economically and environmentally, provided the work is coordinated with the Administration. It is necessary to promote international cooperation in order to improve the efficiency of scientific research in the Zone that facilitates minimization of the aftermath of the Chernobyl catastrophe.

It is necessary to increase the share of scientific research within the scope of work performed in the Zone while providing for expansion of integrated research in order to derive thoroughly scientifically substantiated practical conclusions and measures.

Providing opportunities for developing scientifically substantiated and adequate managerial solutions demands a systemic approach to and generalization of the entire complex of information obtained by various agencies and organizations.

The program of scientific research in the Zone shall determine priorities of basic and applied scientific research and experimental design work along all directions of eliminating the consequences of the Chernobyl catastrophe. The following is planned:

— conducting basic and applied research of the entire complex of problems of eliminating the consequences of the Chernobyl catastrophe in order to derive comprehensive and thoroughly substantiated practical conclusions and develop specific measures;

— functional reciprocal complement of monitoring with scientific research in order to develop models of the condition of and changes in radioenvironmental situations based on a unified factographic Zone system;

— generalization of all information, both the information that has been obtained earlier and information obtained as a result of research performed by various agencies and organizations.

13. Immediate Measures

According to the Concept one must develop an integrated program of work related to bringing the Zone territory to an environmentally safe condition and set stages.

During the first stage it is necessary to implement the following measures:

— perform the division of the Zone into districts in accordance with Concept provisions based on performing specialized environmental mapping in order to predict changes in the situation in the Zone and develop the district-division schedule taking into account changes in the radioenvironmental situation in the Zone;

— perform integrated analysis of the purposefulness and justification of the work performed in the Zone in order to bring it in compliance with Concept provisions and, based on the analysis, make a decision to cease the work that contradicts the Concept.

To optimize production activity and the size of the personnel, it is necessary to do the following:

— create a unified system of activity in the Zone aimed at eliminating the consequences of the Chernobyl catastrophe, and eliminate parallel structures that perform same type assignments;

— reduce as much as possible the size of the personnel in the Zone and remove from the Zone the enterprises and persons whose presence is not called for by basic provisions of the Concept;

— develop a document package regulating the personnel activity, taking into account specific features of the Zone;

— prepare proposals on making changes and amendments to current legislative acts regulating the status of the territory and vital activity of the personnel in the Zone and present them to organizations having the right of legislative initiative;

— implement measures regarding RAW treatment:

— take inventory and investigate the condition of the RWBSs and RWTLSs in order to determine the degree of their environmental safety;

— develop normative documents that would regulate the status of RWTLSs and requirements to their environmental safety;

— implement measures aimed at improving the degree of reliability of localizing barriers of existing RWBSs and ensuring long-term RAW storage in these repositories.

— develop a project of the complex of RAW processing and storage facilities.

It is necessary to develop a unified system for integrated monitoring of the Zone and adjacent territories and implement measures aimed at transforming the "Shelter" facility into an environmentally safe system:

— implement immediate measures for increasing the reliability of the existing "Shelter" facility;

— develop a feasibility study and a project for transforming the "Shelter" facility into an environmentally safe system based on the results of the International Competition.

During the first stage it is necessary to perform design work according to the ChAES decommissioning program and conduct scientific research with integrated analysis of proposed solutions regarding determination of the future fate of the towns of Pripyat and Chernobyl-2.

It is also necessary to develop a feasibility study of water protection measures and justify the need for them according to their anticipated contribution to the reduction of the collective dose and risk, taking into account financial expenditures, and also develop a feasibility study of forestation work in the Zone, taking into account prospects of natural landscape self-restoration, implement a set of measures aimed at increasing the fire safety of forests, and perform organization of forest tracts.

The following work also must be included in the first stage:

— work on the project of completing the perimeter fence to ensure territory protection within the Zone boundaries;

— development of a Zone activity management system, while implementing during the first stage the creation of the automated management system of the Restricted Zone;

— the immediate work related to transforming the town of Chernobyl infrastructure in accordance with the Concept goals and objectives, including improvement of the sanitary-hygienic condition and fire safety of operating municipal service facilities;

— work on returning to the national economy material valuables located in the Zone, including:

— taking inventory of the material valuables and determining their value for future use in the national economy;

— studies aimed at looking for ways to return material valuables located in the Zone to the national economy, taking into account the level of their radionuclide contamination;

— destruction and burial of material valuables that are impossible to return to the national economy (performed taking into account the provisions of this Concept).

— work on bringing unorganized industrial and household waste dumps into the state regulated by normative documents.

It is necessary to develop and implement programs for studying and preserving the historical and cultural heritage of the Chernobyl region and protecting natural landmarks and designating objects of the preserve Zone.

14. Forecast of Environmental Situation in Restricted Zone

14.1. Forecast of Radionuclide Migration Under Extreme Conditions

Water and wind release of radionuclides under extreme weather conditions (floods with not more than a one percent probability, tornadoes, dust storms) and in the case of forest fires will not result in a long-term excess of permissible levels of environmental contamination beyond the Zone boundaries.

Destruction of the "Shelter" facility as a result of an earthquake or human activity, as well as destruction of REBS "Pidlisnyy" and other facilities in the case of flooding can lead to additional radiation contamination of the Zone and adjacent territories.

14.2. Forecast of Environmental Situation in Restricted Zone Up to Year 2050

The area of the forest-covered territory of the Zone will increase to 65-70 percent. Pine forests planted in the 50's, which now form the main part of the forest tracts, will switch to the maturing category and sustain considerable self-thinning. Areas of meadowed fallows will shrink considerably and lose their compactness; the fallows will to a large extent give way to young and middle-age birch and aspen forests and groves. Water meadows too will gradually give way to broad-leaved forests. These changes will facilitate creation of a stable and fire resistant vegetable cover.

The level of groundwater will rise due to self-destruction of amelioration systems and dam building by beavers; marsh-ridden areas will cover at least 10 to 15 percent of the Zone territory.

Areas of continuous contamination will change to dry meadows covered with willow bushes or to dry pine forests if young plantation survives, which will facilitate reduction of the number of dusted territories.

The animal world of the Zone will stabilize quantitatively, and the species composition will shift toward forest species and increased number of predators. It will still be necessary to conduct sanitary-epidemiological control of carriers of tularemia, rabies and leptospirosis.

The density of surface radionuclide contamination of the territory as a whole will decrease gradually due to vertical migration and more or less uniform distribution of radionuclides in the 10 to 30 cm subsurface ground layer and as a result of radioactive decay; cesium-137 and strontium-90 contamination levels will decrease by one to two orders of magnitude, and the probability of air environment contamination with plutonium-239 will decrease three- to tenfold. The role of processes of surface transfer of contamination will decrease substantially as a result of universal creation of vegetation cover. Due to the absence of water runoff the decrease of radioactive contamination on marsh-ridden territories will mainly occur as a result of radioactive decay.

Because of radionuclide filtration through the aeration zone the latter realizes its protective function with respect to groundwater. Part of radionuclide contamination in areas with low aeration zone capacity will go to groundwater; and radionuclide concentration in groundwater in the large part of the Zone will not exceed permissible levels. As a result of filtration and underground runoff of radionuclides the most substantial contamination of groundwater will occur in the near (5-10 km) ChAES zone. Later, radionuclide release with groundwater can become commensurate with surface washout; their concentration will decrease due to nuclear transmutations and stirring, so radionuclide concentration in unloading zones and river valleys will decrease by the end of the forecast period.

The process of gradual radionuclide propagation from local sources located in the most contaminated parts of the Zone into the environment will be taking place. But the scale of radionuclide contamination of the geological environment will depend mainly on levels of area contamination and to lesser extent on the effect of local sources in the vicinity of which will probably form zones of increased radionuclide concentrations in groundwater.

The existing forecasts do not give reason to consider the underground route of radionuclide migration (including migration of strontium-90, the most mobile component) as a significant factor of contamination of the river of Dnieper waters.

Provided the Concept provisions are implemented and due to the anticipated general weakening of processes of surface and underground runoff of radionuclides into the river of Pripyat basin, no deterioration of the radioenvironmental situation in the Zone nor any increased effect of the Zone territory on the radioenvironmental situation in Ukraine is foreseen.

Appendix

List of Legislative Acts and Normative Technical Documents

1. Law of Ukraine "On the Legal Status of the Territory That Sustained Radioactive Contamination as a Result of the Chernobyl Catastrophe".

2. Law of Ukraine "On the Status and Social Protection of Citizens Who Have Suffered As a Result of the Chernobyl Catastrophe".

3. Law of Ukraine "On Environmental Protection".

4. Derzhkomatomnaglyad of Ukraine Resolution of 01-04-92 No. 1 "On Regulating the Safety of Ukraine's Nuclear Power Industry Facilities" (Appendix "List of Rules and Regulations on Safety in Ukraine's Nuclear Power Industry") (a total of 79 titles).

5. Cabinet of Ministers of Ukraine Directive of 02-09-93 No. 88-r "On Social Protection of Citizens Who Moved Without Authorization to the Zone of Alienation of the Land That Sustained Radioactive Contamination As a Result of the Chernobyl Catastrophe".

6. Cabinet of Ministers of Ukraine Resolution of 09-23-93 No. 785 "Regulations for State Environmental Monitoring".

7. "Concept of Population Residence in Ukrainian SSR Territories With Increased Levels of Radioactive Contamination As a Result of the Chernobyl Catastrophe".

8. "Concept of the National Program of Eliminating the Consequences of the Chernobyl Catastrophe for 1994-1995 and for the Period to the Year 2000".

9. "Concept of State Regulation of the Safety and Management of Ukraine's Nuclear Power Industry".

10. "Concept of the National Program of Environmental Protection in Ukraine" (draft).

11. "Concept of Treatment of Ukraine's Radioactive Waste" (draft).

12. "Concept of Decommissioning the Chernobyl AES (Main Provisions)".

13. "Temporary Statute of the Administration of the Zone of Alienation of the Land That Sustained Radioactive Contamination As a Result of the Chernobyl Catastrophe" (approved on 06-02-92 by the Minister of Ukraine on Radiation Protection of the Population From the Aftermath of the Accident at the Chernobyl AES).

14. "Temporary Permissible Levels of Radioactive Contamination for Various Facilities in the Chernobyl AES Zone" No. 32-024/301 of 10-22-90, approved by Deputy Head, 3d Main Directorate, USSR Ministry of Health.

15. "Sanitary-Hygienic and Environmental Requirements to and Criteria for Selecting Land Parcels for Creating Radioactive Waste Burial Sites", approved by First Deputy of the USSR Health Minister on 08-11-89.

16. "Recommendations on the Scope of Control of the Contents of Radionuclides in Organisms of Nuclear Power Plants Personnel", approved by First Deputy of the USSR Health Minister on 07-08-88.

17. "Manual on Calculating Population's Individual Collective Radiation Doses Caused by Releases of Radionuclides Entering the Atmosphere During AES Operation", approved by First Deputy of the USSR Health Minister on 01-25-89.

18. "Methodology Guidelines. Control of Gamma Radiation Doses in Areas Around AESs", approved by First Deputy of the USSR Health Minister on 07-08-88.

19. "Methodology of Establishing a System of Working and Control Levels of Releases of AES IRG," approved by First Deputy of the USSR Health Minister on 03-03-88.

20. "Methodology Recommendations on Sanitary Control of the Contents of Radioactive Substances in Environmental Objects", approved by First Deputy of the USSR Health Minister, 1988.

21. "Recommendations on Controlling Environmental Conditions in Case of Iodine-131 Entering the Atmospheric Air With Industrial Releases", No. 77/3-71.

22. "Individual Protection When Eliminating the Consequences of the ChAES Accident", approved by the Biophysics Institute, USSR Ministry of Health.

23. "Instructions on Using Medicamentous and Decontaminating Agents in the ChAES Accident Area", approved by First Deputy of the USSR Health Minister on 07-25-86.

24. "Instructions on Assessing the Ability to Work of Persons Who Suffered Acute Radiation Injuries", approved by Deputy of the USSR Health Minister on 07-14-80.

25. "Instructions on Diagnostics, Medical Sorting and Treatment of Acute Radiation Injuries", approved by Deputy of the USSR Health Minister on 08-31-77.

26. "Recommendations on Assessing Radiation Consequences of Irradiation of Population During AES Accidents and Premeditated Destructions", approved by First Deputy of the USSR Health Minister on 03-03-88.

27. "Temporary Methodology Recommendations on Organizing and Conducting Professional Psychophysiological Selection of AES Personnel", approved by First Deputy of the USSR Health Minister on 05-10-88.

28. "Plan of Interaction for Prevention and Elimination of the Consequences of Natural Calamities, Accidents, Fires and Other Technogenic in Character Extreme Situations in the Restricted Zone", approved by Minchornobyl on 12-07-92 and by TsO of Ukraine Headquarters on 12-04-92.

29. "Temporary Permissible Levels of Cesium and Strontium-90 Contents in Food and Potable Water, Established Because of the Chernobyl AES Accident", approved by USSR Chief State Sanitary Doctor on 01-21-91.

30. "Instructions and Methodology 'Guidelines on Assessing the Radiation Situation in Contaminated Territories'". Approved by the Methodology Section, the Interagency Commission on Radiation Control of the Environment under the auspices of Goskomgidromet SSSR [USSR State Committee for Hydrometeorology] on 03-17-89.

31. "Manual on Organizing Medical Service for Persons That Have Been Exposed to Ionizing Radiation", Moscow, "Energoatomizdat", 1986.

Coordination List

The "Concept of the Chernobyl Restricted Zone in the territory of Ukraine" has been coordinated with the following Ministries, agencies and organs:

1. Ministry of Environmental Protection and Nuclear Safety of Ukraine
2. Pozhnaglyad Ukrayiny
3. Ts.S. Ukrinvestekspertyzy
4. National Academy of Sciences of Ukraine
5. Forestry Ministry of Ukraine
6. "Chornobylska AES" production association
7. Ministry of Health of Ukraine
8. Derzhatomnaglyad Ukrayiny
9. Minchornobyl Ukrayiny
10. Academy of Agrarian Sciences of Ukraine
11. President's representative, Kiev oblast Administration
12. State Committee of Ukraine for Geology and Utilization of Natural Wealth
13. NKRZU
14. Ministry of Justice of Ukraine

Russia: Three-Dimensional Synthetic Vision System for Robotic 3-D Copier

964D0520A Moscow VESTNIK MOSKOVSKOGO GOSUDARSTVENNOGO TEKHNICHESKOGO UNIVERSITETA: SERIYA MASHINOSTROYENIYE. SPESIALNIY NOMER: "INFORMATSIONNAYA TEKHNOLOGIYA V MEKHANICHESKOM INZHENERSTVE" (Special Issue: "Information Technology in Mechanical Engineering") in Russian No 3, Mar 95 pp 59-64

[Article by S.V. Syrskiy and B.B. Mikhaylov; (manuscript received 2 Nov 94) UDC 621.396]

[FBIS Translated Text]

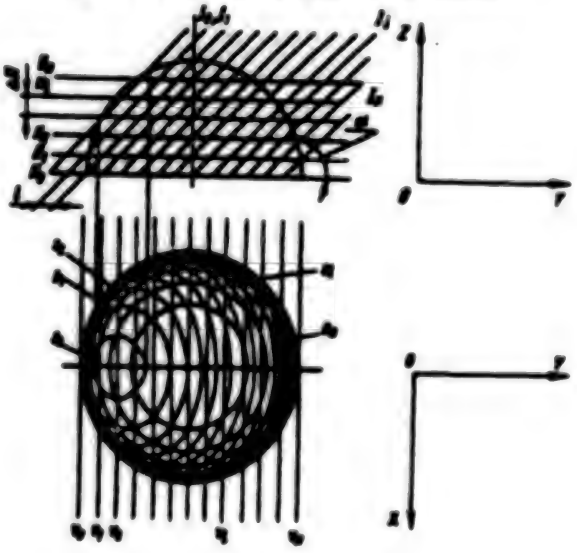
A synthetic vision system is proposed which produces a 3-dimensional image by applying the principle of interferometry. The method of the system's software design, a modification of the hypsometric method, is described and the image processing algorithms are examined. Also the method of designing this system is described and recommendations for selecting the hardware components are given. The specifications for its experimental prototype are included.

Intricate curvilinear surfaces are now being formed on multicoordinate (5,6) universal machine tools or on machine tools with program control, then finished on grinding-profiling machine tools or manually by a fitter/gaugemaker.[1] The main obstacle to automating this process is the difficulty in both specifying the coordinates of target points along the profile of the surface to be machined and then inspecting its actual dimensions. The best way to solve this problem could be the use of contactless measuring systems and, particularly, synthetic vision systems (SVS). The overwhelming majority of now existing SVS's are, however, 2-dimensional or 2.5-dimensional and thus not suitable for determining the dimensions of 3-dimensional objects. At the same time, the few existing 3-dimensional SVS's generally contain several video sensors and require either mechanical or optical scanning of the scene, or intricate algorithms for point-to-point juxtaposition of two images. This contributes to a high cost as well as low speed and poor reliability of such SVS's. The 3-dimensional SVS proposed here operates on the basis of interferometry, using one video sensor and relatively simple image processing algorithms.

Theoretical Basis of the Method. The software for the proposed SVS is based on a modification of the hypsometric method.[2] Accordingly, the object to be copied is being cut by planes $I_1, I_2, \ldots I_n$ inclined to the horizontal base plane H_0 so that the object's surface becomes covered with the contour lines $S_1, S_2, \ldots S_n$

of its cross sections (Figure 1). The points where these contour lines cross vertical planes $V_1,V_2,...,V_n$ (perpendicular to the base plane H_0) are points on the contour lines of the object's intersections by planes $H_1,H_2,...,H_n$ (parallel to the base plane H_0). This is so, because the lines of intersection of the $I_1,I_2,...,I_n$ and the planes $V_1,V_2,...,V_n$ describe the planes $H_1,H_2,...,H_n$ parallel to H_0. By connecting intersection points with the same order number (counting along the OX-axis), one can draw the contour of the object's cross section in a plane H_i. The altitude of the plane of the section H_i above the base plane H_0 is given by the formula $Z= p\Delta H$ (where p- is the order order number of plane V_i relative to the plane which passes through the origin of coordinates; $\Delta H= l \times (\cos \alpha)$ is the distance between two horizontal planes ($H= H_{i+1} - H_i$; L is the distance between two inclined planes; α is the angle between plane I_i and the base plane H_0, i.e., angle of incidence of light ray).

Figure 1. Modified Hypsometric Method



The third coordinate of a point on a curvilinear surface can also be determined by another method, namely by using the distance $Z_i \tan\alpha$ from a point on the intersection of a plane I_i and the object's surface to a point on the intersection of this plane and the base plane H_0 (Z_i is the altitude of i th point on the object's surface above the base plane H_0; α is the angle between plane I_i and the base plane H_0, i.e. angle of incidence of light ray). The altitude of a point on the object's surface is then

$$Z= \Sigma(i= 1 \text{ to } i=n)[d-(y_{i+1}-y_i)\tan\alpha$$

Here: y_{i+1},y_i are the coordinates of points on the section contours S_{i+1},S_i respectively; $d= L/\sin\alpha$; L is the distance between two inclined planes I_{i+1},I_i; α is the angle both planes make with the base plane H_0.

The first method is more convenient for determining the altitudes of individual points on the object's surfaces, the second method is more convenient for plotting the contours of the object's cross sections and determining its geometrical characteristics. One should note that also closed contours I_0 may form on the surface of an object cut by inclined planes (Figure 1). This does not mean that the image processing cannot proceed, but requires more intricate algorithms and causes an image to be less than completely reconstructed. It therefore is desirable to design a SVS so as to avoid formation of closed contours.

The contours of the object's intersections by inclined planes can also be obtained by the conventional method, namely with a light beam shaped by passage through a grating. However, diffraction of light by the elements of such a mask makes formation of narrow light beams difficult and thus renders this method suitable only for qualitative analysis of a scene rather than for determination of the object's dimensions. In view of these problems, it is instead proposed to project interference fringes onto the object's surface. This method requires two sources of coherent light: an object beam and a reference beam. The illuminance at any point is then

$$I= E(1)^2+ E(2)^2+2E(1)E(2)\cos[\phi(1) - \phi(2)]$$

Here: E(1),E(2) and ϕ_1,ϕ_2 are the amplitude and the phases, respectively, of object beam (1) waves and reference beam (2) waves.

The maximum intensity is $I_{max}= [E(1) + E(2)]^2$ and the minimum illuminance is $I_{min}= 0$.[3] The distance between two successive minima (dark fringes) or maxima (bright fringes), i.e., the space period of the interference pattern is $B= \lambda Z/(L \times \cos \alpha)$ when the base plane is vertical and $B= \lambda Z/(L \times \sin \alpha)$ when the base plane is horizontal[4] (λ is the wavelength of light coming from the two sources; Z is the altitude of both light sources above the base plane; L-distance between the two light sources; α is the angle of incidence of light ray). The space period of the interference pattern is regulated by varying either distance L or angle α. The system of coordinates in the plane of the TV camera's photographic plate does not generally coincide with that in the plane of the object and, therefore, determining the coordinates of points of the object requires performing not only the transformation $c_k= Aw_k$ but also the inverse transformation $w_k= A^{-1}$ (c_k and w_k are the matrices of homogenous coordinates of a point in the plane of the

image and in the plane of the object respectively; A and A^{-1} are the matrices of transformation and inverse transformation of coordinates, each of them being the product of four matrices:

1. matrix of optical transformation,

2. displacement matrix of the origin of the camera's system of coordinates moving relative to the camera's fulcrum,

3. rotation matrix of the camera moving relative to the x,y,z axes,

4. displacement matrix of the camera's fulcrum moving relative to the scene's system of coordinates.

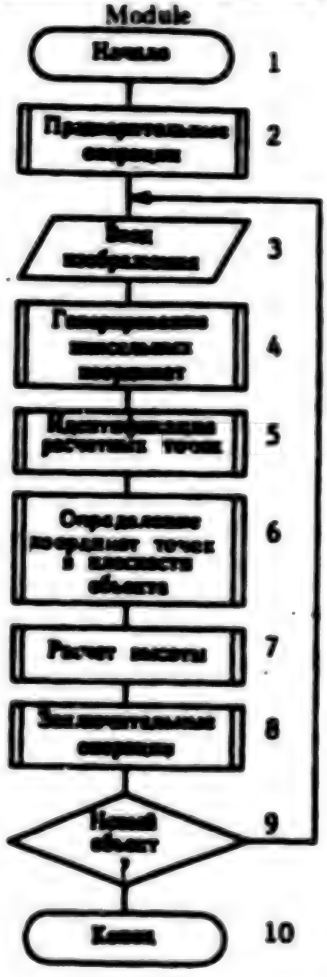
For a unitary rotation matrix we have $x= f[(X-X_0-r_1)/(f-Z-Z_0-r_3)]$ and $y= f[(Y- Y_0-r_2)/(f-Z-Z_0-r_3)]$ in the transform, $X= x[(f-Z-Z_0-r_3)/(f+ X_0+ r_1)]$ and $Y= y[(f-Z-Z_0-r_3)/(f+ Y_0+ r_2)]$ in the inverse transform (where x,y are the coordinates of a point of the image in the camera's system of coordinates; f is the focal length of the camera's objective lens; X,Y,Z are the coordinates of a point of the object; X_0, Y_0,Z_0-displacements of the camera's fulcrum relative to the origin of coordinates in the plane of the object; r_1 ,r_2,r_3 are displacements of the origin of coordinates in the plane of the image along the x,y,z axes respectively. [5] As free Z-coordinate is selected the altitude of the base plane or of the preceding point on the object's surface. For a unitary rotation matrix, image processing is done in the camera's system of coordinates, using whole-number arithmetic. For a nonunitary rotation matrix, (image) processing is done in the object's system of coordinates, the calculations then being made with floating-decimal numbers and thus requiring use of more intricate slower search algorithms for target points. It is, therefore, desirable to avoid use of nonunitary rotation matrices in the SVS design.

Image processing algorithms. Four versions of an image processing algorithm have been devised for the proposed SVS. This so because the SVS can operate with either a multilevel-graded or binary initial image and seek target points in two ways:

1. along minima or maxima lines in the interference fringes (using the first method of determining the third coordinate of a point on the object's surface);

2. over the entire plane of the image (using the second method of determining the third coordinate). The structural scheme of the basic program module (Figure 2) consists of preliminary operations, image data entry, generation of pixel coordinates, identification of target points, determination of coordinates of points in the plane of the object, calculation of altitudes, final operations.

Figure 2. Structural Scheme of Basic Program Module



Key: —1. start —2. preliminary operations —3. image data entry —4. generation of pixel coordinates —5. identification of target points —6. determination of coordinates of points in the plane of the object —7. calculation of altitude —8. final operations —9. new object? —10. end

The preliminary operations include:

1. determining the elements of the transformation matrix;

2. constructing an image of the base plane and storing it in the RAM of the computer;

3. determining the average space period of the interference pattern;

4. determining the minimum intensity difference between two neighboring pixels;

5. determining the coordinates of minima or maxima in the interference fringes, i.e., the base coordinates in the null row in a frame;

6. counting the number of fringes in a frame and determining their angles of inclination to the axes of the camera's system of coordinates.

The elements of the transformation matrix are most conveniently determined by calibration in ordinary diffuse light, using the camera itself as the measuring instrument.[6] The remaining setup parameters are determined on the image of the base plane, after the interference fringes have been projected onto it by methods usually employed for processing images of objects. These methods are subsequently used in the search for target points in systems with a nonunitary rotation matrix, for determining the altitudes of points of the object, in selection of the number of intensity levels for amplitude quantization of that intensity, identification of closed-contour interference fringes. When the search for target points is done along minima or maxima lines in the interference fringes and with a nonunitary image rotation matrix, then the image of the base plane remains stored in the RAM of the computer also after setup of the SVS.

Noise attending spatial discretization and amplitude quantization of a multilevel-graded or binary image is being suppressed during entry of the initial image into the RAM of the computer. This operation is performed with the aid of the TV camera controller.

While pixel coordinates are being generated, there also being determined the points among which target points will then be identified are also being specified. Their identification can be made using a unitary rotation matrix or a nonunitary one and either of the two search algorithms for target points. In the case of a unitary rotation matrix and search over the entire plane of the image one adds the number 1 to the number of scanned points in a row and, when the end of that row has been reached, one adds 1 to the number of rows. In the case of a unitary rotation matrix and search along minima or maxima lines in the interference fringes one adds the number 1 to the number of rows and, when the the last row has been reached, one adds the next numerical value of the base coordinate to the number of scanned points. When a nonunitary rotation matrix is used and search is done along minima or maxima lines in the interferences fringes, then segments of the image of the base plane are convolved with a 3x3-dimensional mask. If at any point of that mask the intensity value is 1 and the coordinates are equal neither to the current ones nor to the preceding ones, this point is selected for its subsequent identification as a target point. When a nonunitary rotation matrix is used and search is done over the entire plane of the image, then the Brazenham algorithm[4] is used for that search.

Identification of target points means verifying that they are located on a minimum or maximum line in an interference fringe. When the system operates with a binary image, then the intensity value at such a point must be 1 and its value at both the preceding point and the following one must be 0. When the system operates with a multilevel-graded image, then as a target point is regarded one at which the intensity level is lower than at both the preceding point and at the following one. The pixel coordinates of the target points are entered into the buffer memory of the computer for subsequent operations.

For determining the coordinates of points in the plane of the object, their pixel coordinates are multiplied by the rate of the camera's scanning raster and by corresponding elements of the transformation matrix. As free coordinate Z, the altitude of the preceding point when the object ascends or the altitude of the following point when the object descends is selected.

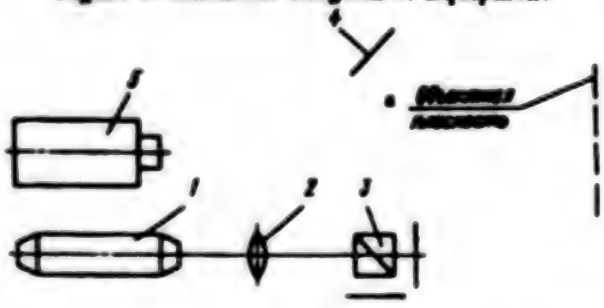
During the target points identification stage, as a preliminary step prior to calculation of their altitudes, there are first determined either their order numbers along each minimum or maximum line in two neighboring interference fringes (using the search algorithm along these lines) or the distance between these two fringes, i.e., the period of the interference pattern (using the search algorithm over the entire plane. Then, for determining their altitudes in the system of coordinates in the plane of the object, their pixel coordinates are also multiplied by the rate of that raster and by corresponding elements of the transformation matrix - with the only difference that, here, displacement of the origin of coordinates in the plane of the image is ignored. The same numerical value is assigned here to the free coordinate as in determination of coordinates of points in the plane of the object.

During its operation the proposed system sometimes encounters unusual situations in which it is difficult to determine unambiguously the coordinates of a target point of the object. Various means of resolving indeterminacies have, therefore, been provided in the system. After the coordinates of points of the object have been determined, they must be converted into a form convenient for further handling. An example is the format of the AUTOCAD program package, in which data processing can then proceed. The image of the object can also be displayed on the screen of a video controller in the form of a grid (mesh) of this package or as an approximation of its surface with triangles (triangulation), and then corrected by the system user. When the system operates

as a component of a robototechnological facility, then the dimensions obtained as a result of such processing are compared with the dimensions on the blueprint depicting the profile of the given curvilinear surface and the errors are then converted into control signals for the robot drives.

Hardware. The proposed SVS uses the same hardware as that of simple 2-dimensional ones. It also consists (Figure 3) of: a light source 1, a beam expander 2, an interferometer 3, a plane mirror 4, and a TV camera 5 with a video controller. This being a 3-dimensional system, however, it must meet some specific requirements. These will be discussed as they apply to each component device individually.

Figure 3. Schematic Diagram of Equipment



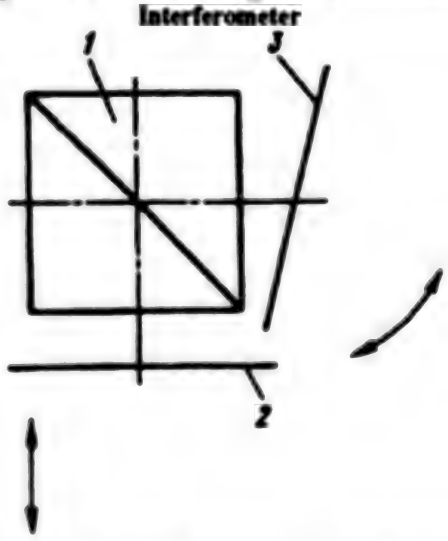
Key: —1. light source —2. beam expander —3. interferometer —4. plane mirror —5. TV camera with video controller —a. plane of object

Light source. The main requirement the light source must meet is emission of highly coherent and adequately powerful radiation. This requirement is most closely met by helium-neon gas lasers, their outstanding features being not only high stability and high reliability but also relatively low cost. In order to maximize the period of the interference pattern, it is desirable to select a red or infrared laser.

Beam Expander. The diameter of a laser beam is very small (the beam of an AG-66 laser is 1.1 mm in diameter) and, therefore, it must be expanded for illumination of a scene. A conventional beam expander is a short-focus microlens. Its focal length is $f = r_0 L/S$ (r_0, (0.25d is the radius of the emitted beam, d is the diameter of the light spot produced by the laser beam on a black dull surface. L is the distance from the focus of the lens to the plane of the object, S is the maximum radius of the light spot in the plane of the object as shown in Figure 3. The intensity at the edge of a scene edge is then $I = P/(\pi eS)$ (P is the laser output power). [4]

Interferometer. The interferometer splits the light beam into a object beam and a reference beam, for subsequent formation of moire' fringes. The simplest interferometer suitable for use in the proposed system is a plane-parallel plate placed at the total-internal-reflection angle to the incident light beam. The period of interference pattern is then $B = \lambda Z/(L \cos \alpha)$ for a vertical base plane and $B = \lambda Z/(L \sin \alpha)$ for a horizontal base plane (λ is the wavelength of the light; Z is the altitude of light source above the base plane; L is the thickness of the plane-parallel plate; α is the angle of light beam incidence). More convenient to use, however, is a Michelson interferometer (Figure 4) consisting of a beam splitter cube 1, a parallel-movable mirror 2, and a rotatable mirror 3. Mismatch between the two interferometer arms is regulated by forward or backward movement of mirror 2, this being analogous to varying the thickness of the beam splitter. The angle of light beam incidence, and thus the period of the interference pattern, are regulated by rotation of mirror 3.

Figure 4. Schematic Diagram of Michelson Interferometer



Key: —1. beam splitter cube —2. parallel-movable mirror —3. rotatable mirror

Plane Mirror. This mirror is needed for varying the direction of the light beam. It must have a high-quality surface finish, to ensure that no spurious fringes appear in the plane of the image.

TV Camera With Video Controller. The camera records the image and the video controller converts the video signals into a form suitable for processing by computer. How their parameters are selected determines how accurately the coordinates of points of the object will

be determined and how completely the image will be reconstructed. The error of measurement of the coordinates depends on the discretization step in the camera or in the video controller. In operation with a multilevel-graded image this error is equal to one step. In operation with a binary image it is equal to two steps, considering that there are unusual situations. In the object's system of coordinates this error is $\Delta X = \Delta x(f-Z_0)/f$. In the case of a nonunitary rotation matrix the error is estimated at the most unfavorably located point, usually at the edge of the scene. The number of gradation levels for amplitude quantization in a system with a multilevel-graded image is selected on the basis of the minimum illuminance difference between two neighboring pixels.

System Configuration. When designing a SVS, it is necessary to select a configuration which minimizes the error of determination of coordinates. The error will be minimum when the altitudes of two neighboring target points of the object differ by not more than the distance between two pixels, which is achieved by either mounting the camera at an appropriate altitude or selecting an appropriate period of the interference pattern. The altitude gradient is

$$Z = f[\Delta x(f-Z_0)-XZ]/[\Delta x(f-Z_0)-fX]-Z$$

and the corresponding period of the interference pattern is

$$\Delta x = fX(f-Z_0)/(f-Z_0)(f-Z_0)$$

Here: f is the focal length of the objective lens; X,Y are coordinates of a critical point on the scene, Z_0 is the altitude of the camera above the base plane.

Computer. Selection of the computer is based on knowledge of two of its characteristics: speed and RAM capacity. In our case the RAM is used for storage of information coming from the video controller, intermediate results of processing, and certain special programs. The required speed of our SVS depends on the characteristics of the equipment connected to it and its actual speed depends on the number of the various kinds of operations it must perform in processing one frame.

The proposed system processes in one frame a 50x50 mm² large surface segment within a time of 0.05-1.5 s with a 0.1 mm precision, the capacity of the RAM it needs for this being within the 13-105 kbyte range depending on the kind of image processing algorithm. These performance characteristics can be improved by use of more advanced equipment. With the aid of this system, moreover, it is possible to determine the mass-inertia characteristics of objects and the space coordinates of their centers of gravity, and to also perform image recognition operations.

Bibliography

1. A.G. Kosilova and R.K. Meshcheryakova (editors), Machine Design Engineer's Handbook, Vol 1; Izd. Mashinostroyenie, Moscow 1985, p. 512.

2. V.M. Ginzburg and B.M. Stepanova (editors), Holography: Methods and Apparatus; Izd. Sovetskoye Radio, Moscow 1974, p. 211.

3. G.S. Landsberg; Optics; Izd. Nauka, Moscow 1976, p. 617.

4. R. Jokes and K. Wykes, Holographic and Speckle Interferometry; Izd. Mir, Moscow 1986, p. 410.

5. K. Fu, R. Gonzales, and K. Li, Robototechnology; Izd. Mir, Moscow 1989, p. 600.

6. L. Ammeral, Machine Graphics on Personal Computers, Izd. "Sol Sistem", Moscow 1992, p. 225.

Ukraine: Cylindrical Shell Stability Under Constrained Deflections, One-Sided Constraints

964D0554 Kiev PRIKLADNAYA MEKHANIKA in Russian Sep 95 No 9, pp 46-50

[Article by S.N. Konyukhov, Yu.M. Mulyar and Yu.K. Privarnikov "Yuzhnoye" Design Bureau, Dnepropetrovsk, Ukraine; (manuscript received 6 May 94) UDC 539.3]

[FBIS Summary] The authors studied the stability of a cylindrical shell in the case of one-sided constraints. By solving neutral equilibrium equations in a linear formulation, they derived analytical expressions for critical values of the axial force and external pressure. The derived values are in sufficient agreement with experimental data. It is noted that the derived formulas for determining critical loads do not cover the entire spectrum of design of one-sided constraints used in the experiments; therefore, for theoretical substantiation of extensive experimental data and better understanding of the phenomenon of buckling, further studies are needed. Figure 1, references 6: all Russian.

Russia: Electric Model of Solid-State Wave Gyro

964D0553 Moscow IZVESTIYA ROSSIYSKOY AKADEMII NAUK: MEKHANIKA TVERDOGO TELA in Russian No 5, Sep-Oct 95 pp 12-24

[Article by V.F. Zhuravlev and D.D. Linch, Moscow; (manuscript received 17 Feb 95) UDC 531.383]

[FBIS Summary] The effect of electrical processes in the resonator and in control, information reading and excitation electrodes on the evolution of standing waves in a gyro is studied. Electrical and mechanical oscillations are examined in their interdependence. It is

demonstrated that, as a result of this interdependence, standing waves in an ideal device undergo all types of evolution—breakdown, precession, and amplitude and frequency changes. The discovered effects have regular character and can be taken into account in information processing algorithms. The authors constructed an electric model of a solid-state wave gyro with three types of electrodes—information reading electrodes, standing waves control electrodes, and a ring electrode for maintaining resonator oscillations. One can reduce the effect of electrical processes on waves in the resonator by changing the method of maintaining oscillations. Figures 3, references 3: 2 Russian, 1 Western.

Belarus: EPR-Spectroscopy of Iron, Manganese, Copper Ions; Radiation Centers in Multicomponent Glasses, Crystalline Glass

964D0721 Minsk ZHURNAL PRIKLADNOY SPEKTROSKOPII in Russian
No 6, Nov-Dec 95 pp 150-156

[Article by S.V. Stefanovskiy, Moscow "Radon" Scientific Production Association, 7th Rostov Lane 2/14, 119121, Moscow, (manuscript received 4 Oct 94) UDC 621.039.73]

[FBIS Summary] The objective of the work was to study the structural position of iron, manganese and copper ions and identify paramagnetic radiation centers in glass-like materials containing actual ash residue of incinerated radioactive waste. The experimental procedure is described, and experimental results are presented and discussed. The author used IR- and EPR- [electronic paramagnetic resonance] spectroscopy. The presence of organic compounds in the ash residue indicated that its vitrification was taking place under reduction conditions, which must have considerable effect on the status of materials oxidation and their structure and properties, and in the end on reliability of radionuclide immobilization. Figures 2, tables 1, references 12: 9 Russian, 3 Western.

Ukraine: Tooth Defects Linked With Chemical Burial Site

964D1054

[FBIS Report] The newspaper PRAVDA-5 (No 14, 12-19 Apr 96 p 10) reports a theory that unusual dental deformities occuring in large numbers of children in a Ukrainian town may have been caused by military chemicals buried nearby. The account gives a detailed description of the burial site.

According to PRAVDA-5's sources, the problems with the children's teeth were first noted shortly after the military buried unknown liquid chemicals near Sosnovka, a mining town with a population of 10,000, located 100 kilometers from Lvov. Unnamed witnesses told reporter Aleksandr Golub that the military, working primarily at night, dug a large pit in a clearing in a dense pine forest outside Sosnovka and laid out "unusually wide asphalt roads. . . clearly not inferior to city streets" running directly to the pit. Eyewitnesses reportedly observed "columns of military tank trucks," presumably transporting liquid chemicals to the site (1).

Mysterious Syndrome

The dental problems have reportedly been observed only in Sosnovka (1), and only since 1989 (4). An exhaustive screening of local schoolchildren found that over 1000 had discolored, lustreless teeth that crumbled easily. Only a handful of the younger school children were free of the disorder (1). Teeth which developed before or after the children lived in the village are normal, a fact that suggests an environmental cause. Initially, the defects were found only in children seven to ten years old, but recently they began to appear in milk teeth (1). Nearly all the victims also complain of pain in their legs.

Although press accounts refer to the dental defects as hypoplasia, or underdevelopment of the enamel — a condition usually resulting from such influences as disease, vitamin deficiency, and medications — the massive numbers of children involved prompted medical investigators to consider unusual causes (1). Galina Solenko, a junior researcher at Lvov Medical Institute's Department of Pediatric Dentistry told a TRUD reporter that "preliminary data indicate that we have most likely encountered an unknown disease caused by chemical substances" (2). Scientists are studying possible connections to high levels of fluorine or heavy metals in the drinking water, atmospheric pollution from ore concentration plants, or overuse of fertilizers. Another theory blaming improperly constructed slag heaps at local plants was dismissed as improbable by TRUD reporter German Klyucherov, who noted that such conditions exist elsewhere, but the syndrome is unique to Sosnovka (2).

Echoes of Chernovtsi

Some commentators found the Sosnovka disorder reminiscent of an outbreak of alopecia (baldness) that occurred in Chernovtsi, Ukraine in 1988-1989 (2,4). In addition to hair loss, the Chernovtsi victims, all of them two- to four-year-olds, experienced a wide range of symptoms including neurological problems, lesions of the oral mucosa and respiratory distress (5). Many of them had joint pain, and a few had discolored teeth, attributed to excessive fluorine (6). Although many experts thought thallium poisoning was responsible for the Chernovtsi syndrome, some thought that the children had been poisoned by inhaling an unknown, complex, chemical compound (6,7), probably a high-density gas containing boron, that may have come from a plant that made bricks out of industrial wastes (6). A similar outbreak of alopecia in 200 Sillamae, Estonia children was attributed to a fire at a shale mine (8,9).

Investigation, Aid Demanded

The Sosnovka patients' families are afraid that the damaged teeth may be the first sign of more serious, environmentally caused health problems. They want the state to declare the area a disaster zone and provide free expert medical examinations and treatment (5). Local governments and a trade union group have been actively seeking the oblast and republic governments' attention to this problem with some success (3):

— The town councils of Sosnovka and nearby Chervonograd successfully petitioned the Ukrainian Ministry of Environmental Protection and Nuclear Safety to start an investigation.

— The Chervonograd executive committee petitioned the Lvov Oblast Public Health Department special commission on Sosnovka to take protective measures pending the results of the study. The Lvov Oblast Administration for Ecological Safety was working with the Health Ministry to decide on further action.

— The regional association of the Independent Miners' Trade Unions of Ukraine appealed to the Ministry of the Coal Industry for 5 billion karbovantsy for equipment and medicines for the children.

In surprising contrast to their efforts to win higher level aid for the affected children, the Sosnovka town administration reportedly plans to build an additional 15-hectare dump near Sosnovka, on the site of a Polish village destroyed during World War II. Although geologists have warned that the ground is unsuitable for this use and that wastes from the new dump will

leach into the Bug River (1), the town administrators reportedly are proceeding with the project because they believe it will be "extremely profitable."

Sources

1. Moscow PRAVDA-S No 14, 12-19 Apr 96 p 10

2. Moscow TRUD 12 Aug 96 p 1

3. Kiev ZA VILNU UKRAYINU 14 Nov 95 p 3

4. Kiev HOLOS UKRAYINY 26 Sep 95 p1

5. Kiev VRACHEBNOYE DELO No 8, Aug 81 pp 88-91

6. Moscow NAUKA I ZHIZN No 1 Jan 91 pp 26-29

7. Moscow TRUD 4 Mar 93 p 2

8. Moscow PRIRODA No 2 Feb 93 p 24-29

9. Moscow NEZAVISIMAYA GAZETA 7 Feb 92 p 6

Russia's Pharmaceutical Market: Structure, State, and Prospects for Development

964D0533A Moscow FARMATSIYA in Russian May 95 Vol 44 No 5, pp 8-10

[Article by A.N. Uzdenikov, "Lekarstva Rossii" (Russia's Drugs) Trading House Joint-Stock Company]

[FBIS Translated Text] By 1995 Russia's pharmaceutical market changed fundamentally as compared with the first two years of reforms, when it had just begun to be formed and in many respects repeated the planned-distributional system of supply through the traditional network of state pharmaceutical enterprises and institutions.

At present most of the received medicinal substances are products of nonstate enterprises and foreign firms. In the wholesale link the delivery of these resources to pharmaceutical institutions has also passed to independent distributors with private or mixed forms of ownership, the volume of output of which in the total turnover already occupies 60 to 70 percent, while the output of state pharmaceutical state organizations, 30 to 40 percent of the turnover. Most of the pharmacies have become independent juridical persons, although, basically, they have remained municipal and state pharmacies. More and more pharmacies of various firms and of private commercial enterprises appear in the retail link. Small retail pharmaceutical institutions—pharmaceutical stations and kiosks—established by wholesale dealers in order to accelerate the sale of the limited list of the most popular medicinal substances and other medical and incidental goods have become especially widespread.

In Russia about 110 enterprises produce medicinal substances and articles for medical purposes and 42 institutes and production facilities, immunobiological preparations. In 1994 medical products worth 2.36 trillion rubles, including medicinal substances worth 1.63 trillion rubles, were produced. This ensured about 40 percent and, with respect to immunobiological preparations, 100 percent of the orders of the regions' medical and pharmaceutical service. The list of produced medicinal substances includes about 2,500 items.

Medicinal substances and articles for medical purposes worth 1.3 billion U.S. dollars (or 5 trillion rubles) were imported into Russia in 1994. The list of foreign medicinal substances registered in Russia at the end of 1994 totaled about 4,500 items and continues to expand. To be sure, the list has many of the same medicinal substances with different names, but not all of them are imported into Russia.

The RF Ministry of Health Care and the Medical Industry estimated the volume of the pharmaceutical market in 1995 at 8 trillion rubles (in prices at the beginning of 1995).

However, retaining the level of production and import of medicinal substances, effective demand for medicinal substances in Russia can be met fully.

At the same time, the results of an analysis of the structure of the pharmaceutical market and of its provision with financing based on state guarantees show that serious interruptions in providing patients with many medicinal substances can recur.

In accordance with the existing presidential edicts and decrees of the Russian Government more than 60 percent of the total volume of medicinal substances should be released to the population at the expense of the budget and extrabudgetary sources of financing. At the same time, such specific groups of medicinal substances as antitumoral, antituberculotic, and antidiabetic and medicinal substances used for the treatment of asthma and mental, some cardiovascular, endocrine, and a number of other diseases should be released to patients in a full volume free of charge. According to the data of the RF Ministry of Economics, there are more than 30 million such patients. Furthermore, patients in hospitals, children under the age of three, invalids of the Great Patriotic War, persons equated with them, who suffered from nuclear tests and the accident at the Chernobyl AES (nuclear electric power station), nationalities of the Far North, and a number of other population groups should receive all medicinal substances free of charge. Discounts of 50 percent of the cost of medicinal substances have been set for outpatients—invalids of group II and war veterans—and, with regard to the

list of vitally necessary and the most important medicinal substances, medicinal substances should be released to Russia's entire population at a discount set by bodies of executive power in regions.

In connection with this federal and regional state bodies in their budgets and in budgets of mandatory medical insurance funds should provide for about 5 trillion rubles (in prices at the beginning of 1995). This is the state sector of the pharmaceutical market.

The practice of past years and of the current year shows that budgets at all levels and mandatory medical insurance funds do not have capital in such volumes. Therefore, the procedure for the release of the indicated medicinal substances has not been confirmed by financing and effective demand and they will not arrive at the country's pharmaceutical market in sufficient quantities. In 1994 the needs of the RF Ministry of Health Care and the Medical Industry for the financing of medicinal care were met 70 percent. That is why in Russia last year the production of psychotropic, antitumoral, and cardiovascular medicinal substances and substances for narcosis and anesthesia decreased by 30 to 40 percent and of antituberculotic medicinal substances, to less than one-seventh, while the total decline in production was 5.4 percent. That is why medicinal substances of the indicated groups are received from foreign firms in extremely limited amounts. These firms are unable to receive payment for delivered medicinal substances used in 1991-1993, which are worth hundreds of millions of U.S. dollars.

The free trade sector, in which medicinal substances are paid for by outpatients from their own funds, is estimated at 3 to 3.5 trillion rubles. This sector of the pharmaceutical market is filled with medicinal substances of domestic production and with those imported in quantities exceeding the need 1.5- to 2-fold.

These discrepancies are connected both with the unsound policy contradicting market laws by a number of public health managers at all levels with respect to the expansion of a free and preferential release of medicinal substances to patients without confirmation and with the complete chaos in the use of most of the released budgetary and extrabudgetary funds for these purposes. Thus, the 1995 government decree on the Implementation of the Law on Veterans establishes that the selection and prescription of medicinal substances and norms of their release on favorable terms are determined by the attending physician. This, in fact, confirms the practice of an uncontrolled prescription by a physician and receipt by outpatients of all medicinal substances without due regard for their cost. Precisely this leads to an unpredictable rise in expenditures on medicinal care, which require ever greater appropriations from the budget and from mandatory medical insurance funds. As a result, in the last three years the share of expenditures on the payment for medicinal substances in total public health appropriations has increased from 10 to 25 percent and in a number of regions, to 30 percent.

In connection with the above-stated there is a need for urgent measures to regulate the situation in the state sector of the pharmaceutical market. On the basis of the existing experience in Russia's individual regions (Ryazan Oblast, Yekaterinburg, Rostov-on-Don, and so forth), as well as of international practice, it is necessary to implement a number of measures:

1. To establish standards of treatment of basic types of diseases and on their basis to form lists of medicinal substances for inclusion in orders for state needs. As practice shows, it is advisable to organize such work at all levels, beginning with the federal level and ending with general health institutions. For now the initiative belongs to individual regions. According to the proposals by the administration of a number of regions, with the participation of the federal mandatory medical insurance fund (Kaluga, Rostov-on-Don, Yekaterinburg, and the Komi Republic), the RF Ministry of Health Care and the Medical Industry, and the Russian Center for Pharmaceutical and Medical-Technical Information and with the assistance of the U.S. Agency for International Development in the introduction of the project "Efficient Pharmaceutical Management" (Ryazan, Pskov, and Novgorod oblasts), work is being done on the transition to a controlled expenditure of medicinal substances paid for out of state sources of financing.

The first experience in the formation of lists of medicinal substances for mandatory use in the treatment of patients in state general health institutions and of records of these lists and the organization of the collections of orders of hospitals and polyclinics make it possible to solve the following problem:

2. To regulate the organization of supply. For this purpose tenders (contests) are held for the delivery of medicinal substances included in lists by firms and manufacturing enterprises (or wholesale dealers). The results have shown that such an organization of supply makes it possible to significantly reduce the list of medicinal substances purchased with state funds without a deterioration in the quality of treatment and to ensure deliveries of medicinal substances at stable optimum prices.

3. On the basis of a stable list, order volumes, and prices to have forecast expenditures, which should be specified in the budget of territories and the mandatory medical insurance fund.

The need for the most rapid organization of this work is dictated by the fact that at present the domestic industry produces medicinal substances at prices much lower than those of foreign analogs. At the same time, foreign firms offer Russia 2.5-fold more medicinal substances. Many of them are synonyms or analogs, but greatly differ in prices.

The regulation of this section of medicinal supply will eliminate the possibility of corruption, ensure complete openness during the preparation of orders and conclusion of contracts and deliveries, eliminate numerous intermediary links, and ensure maximum control over the distribution and expenditure of received medicinal substances, which will also eliminate the possibility of abuses when medicinal substances are prescribed and received according to free-of-charge and preferential prescriptions.

The regulation of the use of the list of medicinal substances in the state sector of the pharmaceutical market and the stabilization of prices of medical products delivered within the framework of the order for state needs guarantees a reduction in expenditures on the purchase of medicinal substances and ensures the possibility of state control over the expenditure of assigned appropriations.

Other approaches should be applied in the free trade sector, where internal and borrowed funds of manufacturers and wholesale dealers are used. Work is carried out by them with a risk of sale on the market. Competition and openness and provision of the same conditions for activity for all participants are the main conditions for the stabilization of this sector.

At present more than 150 industrial enterprises, about 3,500 wholesale dealers and agencies of foreign pharmaceutical firms, and more than 15,000 retail pharmaceutical institutions have joined the participants in Russia's pharmaceutical market. State regulation of their work is limited only to the procedure for the control of the quality of medicinal substances, price formation rules, training and control over the staffing with specialists, licensing of their activity, and issue of permits for the import and export of medicinal substances. With respect to organization a coordination of the production activity of these enterprises and legal protection against officials' arbitrariness are virtually absent.

The establishment of uniform "rules of the game" for participants in the pharmaceutical market and the creation of conditions for the protection of their property and production rights are possible only through their unification on a voluntary basis in accordance with existing legislation.

The realization of such an idea in Russia was carried out on the initiative of 24 participants in the pharmaceutical market (production enterprises, wholesale dealers, and pharmacies). They have established the FarmAsK Association of Commercial Pharmaceutical Organizations, the bylaws of which provide for the coordination of the activity of its participants, protection of their interests in all instances, and organization of scientific, educational, consultative, and a number of other services at the requests of association members.

All these measures will make it possible to change over from a spontaneous, little controlled market to a civilized market subject to Russia's laws.

Russia: Optical Breakdown and Explosive Boiling in Response to Laser Radiation Pulses Acting on Pigmented Biological Tissue

964D0760A Moscow IZVESTIYA AKADEMII NAUK SERIYA FIZICHESKAYA in Russian Jun 95 Vol 59 No 6, pp 76-83

[Article by V. K. Pustovalov, Belarusian State Polytechnical Academy; UDC 621.373]

[FBIS Translated Text] **An analytical model of heating of a pigmented spherical granule in biological tissues by a laser radiation pulse is proposed. The model permits estimation of threshold energies or radiation intensities initiating optical breakdown, explosive boiling of water, and selective thermal denaturation of granules. The results of calculations using the model are compared with experimental data, and the agreement is satisfactory.**

Lasers have recently enjoyed extensive and effective application in different fields of medicine such as ophthalmology, dermatology, heart surgery etc. In ophthalmology for example, laser pulses are used on the retina, to perforate tissues of the interior division of the eye in glaucoma treatment, and so on [1-5]. Investigation of the interaction of short laser pulses within a range of variation of lengths $10^{-4}<t_i<10^{-3}$ sec with pigmented biological tissues of the eye containing granules of different pigments is of special interest. This paper analyzes heating of a pigmented granule by a laser radiation pulse, and compares the calculation results with experimental data.

Let a beam of optical radiation with wavelength λ propagate in tissues of the eye along axis X in a cylindrical coordinate system X, R. Tissues of the eye are a complex multilayered heterogeneous structure, as modeled in Figure 1 [3]. Axis X, which coincides with the beam axis, is normal to the interface of tissue layers, and the characteristic thickness of the layers is 10-100

μ. The distribution of radiation intensity I with respect to the beam cross section is assumed to be Gaussian:

$$I(X, R, t) = I_0(X, t) \exp(-R^2/R_0^2), \quad (1)$$

where I_0—maximum intensity on beam axis, R_0—characteristic beam radius, which may depend on X, t—time. Pulse energy on the cornea Q_0 (X=0) for a radiation beam unlimited with respect to R is determined by the expression

$$Q_0 = \int_0^\infty dt \int_0^\infty I(X = 0, R, t) \cdot 2\pi R dR. \quad (2)$$

For short radiation pulses with length t_0 10^{-4} sec, the form of the relationship of radiation intensity to time does not for practical purposes affect the results [4], and therefore we can assume intensity I_0 to be constant over the time of the pulse's action. For constant intensity during the pulse and for an unlimited Gaussian beam, (1) and (2) give us

$$Q_0 = I_0(X = 0) \pi R_0^2(X = 0) t_0. \quad (3)$$

Relationship (3) may also be used in the case of uniform intensity distribution over an irradiated spot with radius R_0. The geometric and optical parameters of the different layers of the eye were taken from [3], while the thermophysical properties of the layers were taken from [5]. When radiation propagates from the cornea (pupil) to the retina (the pigmented epithelium), it undergoes a certain amount of weakening in transparent ocular media, and the pulse energy at the retina Q_r is equal to

$$Q_r = I_0(X_0) \pi R_0^2(X_0) t_0 = T_\lambda Q_0, \quad (4)$$

where T_λ is transmission of radiation with wavelength λ by transparent ocular media.

A significant feature of one of the layers of ocular tissues—the pigmented epithelium (PE)—is its granular (heterogeneous) structure. A PE layer with characteristic thickness approximately equals5-10 μ contains pigmented melanoprotein granules of spherical and spheroidal shape with a characteristic size of approximately equals1 μ. These granules are also found in skin and other tissues, and they determine the degree of pigmentation and coloring of biological tissues. In this case the granules selectively absorb up to 90 percent of the energy of laser radiation absorbed by the PE layer, while surrounding biological tissues usually have a much lower absorption coefficient. In response to radiation pulses the granules overheat considerably relative to the environment, and transfer their energy to surrounding biological tissues by thermal conductivity.

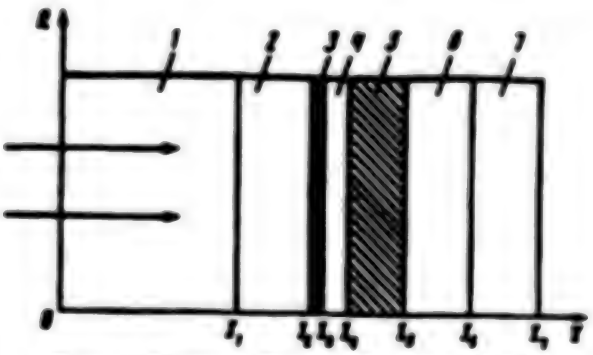


Figure 1. Diagram Showing Layers of Ocular Biological Tissues [3]:

—1. transparent ocular media, —2. neutral epithelium (retina), —3. pigmented epithelium (PE), —4. capillary layer of vascular membrane, —5. pigmented layer of vascular membrane, —6. vascular membrane, —7. sclera. Arrows indicate direction of propagation of radiation

Heat exchange of spherical and spheroidal granules with the environment in response to radiation was investigated in [6,7]. The need for accounting for the granular structure of the pigmented epithelium when considering the effect of radiation pulses with duration $t_0<10^{-3}$ sec and with threshold values of energy Q_{0*} measured at the cornea and leading to the appearance of an ophthalmoscopically observed focus of thermal denaturation with a characteristic size of approximately 20-30 μ with a probability of around 50 percent, was established in [7,8] on the basis of numerical solution of the derived equation system. A possibility was also shown for selective thermal denaturation of pigmented granules by radiation pulses with $t_0<10^{-3}$ sec and with particular pulse energies at the cornea Q_{0*}, when thermal denaturation occurs only within the granule volume, without formation of a continuous macroscopic focus in the volume of biological tissue, and the proportion of heat-inactivated molecules within the granule exceeds 50 percent [7,8].

Because granules are the principal absorbers of radiation energy in the pigmented layer, it is obvious that processes of lowest threshold (with respect to energy) will begin in the granules. When pulses of intensive radiation are rather short, heating of the granule and the water-containing biological tissue surrounding it may occur at rates of approximately 10^8-10^9 K/sec. In this case water surrounding the granule may assume metastable state, reaching the temperature of explosive boiling, above which very fast (explosive) boiling of volumes of water that are far into the metastable region begins.

With further growth of the energy of short pulses of laser radiation, optical breakdown and plasma formation may occur in biological tissues. In the presence of these processes, the steam envelope forming on the granule or the plasma cavity expands to create a powerful pulse of pressure in the surrounding biological tissue, which may cause mechanical damage and rupture biological tissues. Explosive steam formation and optical breakdown occur at minimum threshold intensities precisely in pigmented biological tissues containing pigmented granules that absorb radiation energy, and not in homogeneous biological tissues not containing such granules.

Energy values Q_{ec}, Q_{ec}, Q_{ec}, measured at the cornea (c) and leading respectively to formation of a granular (g) and ophthalmoscopically (o) observable focus of thermal denaturation, and to steam formation (s) on granules, were obtained in [9-11] by numerically calculating complex nonlinear equation systems that include equations for radiation transport, the thermal balance of spherical and spheroidal granules with regard for unidimensional thermal conductivity, an equation for two-dimensional thermal conductivity for the entire volume of biological tissue, an equation for one-dimensional hydrodynamics for the steam envelope, and so on.

On the other hand it would be highly interesting to obtain rather simple analytical relationships with which to estimate the characteristic threshold energies of a radiation pulse that lead to the appearance of certain physical processes initiated on pigmented granules absorbing radiation energy. The situation is also simplified by the circumstance that as calculation of the complete equation systems showed, the start of the process's development in the case of short radiation pulses may be considered with a model of a single granule [9-11]. Processes such as explosive steam formation and optical breakdown (plasma formation) are threshold processes—that is, there is a certain laser pulse energy (energy density) beginning with which this process develops. Obviously the threshold energy also determines the threshold temperature value of the granule to which it is heated by the laser radiation pulse. To determine threshold energies we will utilize some characteristic values of the threshold temperatures of heating of the granule volume or its surface.

To describe absorption of the energy of a radiation pulse and heating of a spherical granule with radius r_0 in an approximation assuming uniform temperature T_0 through its volume and quasi-stationary heat exchange of the granule with surrounding biological tissue, we use the following equation [10,11]:

$$\rho_0 V_0 C_0 \frac{dT_0}{dt} = \frac{1}{4} I_0(X_0) K_\lambda S_0 - j_\Delta S_0 \qquad (5)$$

with the initial condition

$$T_0(t = 0) = t_\infty, \qquad (6)$$

where ρ_0, C_0—density and heat capacity of the substance of the granule; $V_0=(4/3)\pi r_0^3$, $S_0=4\pi r_0^2$—volume and surface area of a spherical granule with radius r_0; T_∞—initial temperature of the granule and biological tissue; $I_0(X_0)$—intensity of laser radiation at the location of the granule on the PE boundary; K_λ—factor accounting for the effectiveness of absorption of the energy of radiation with wavelength λ by a spherical granule with radius r_0. The flow density of heat j_Δ drawn off from the granule by the mechanism of nonlinear thermal conductivity is determined in the quasi-stationary approximation when a is not equal to -1 by the expression [7,10]

$$j_\Delta = \frac{k_\infty T_\infty}{(a+1) r_0}\left[\left(\frac{T_0}{T_\infty}\right)^{a+1} - 1\right], \qquad (7)$$

where the coefficient of thermal conductivity of the surrounding biological tissue k is given as $k=k_\infty(T/T_\infty)^a$, where K_∞, a—some constants; T—temperature of the biological tissue.

Equation (5) uses an approximation of homogeneous heat evolution in the granule volume due to absorption of radiation energy, which holds when $r_0<\lambda$. The characteristic time t_1 of heat exchange by a single granule with the environment is $t_1$approximately equalsr_0^2/4χapproximately equals3.6 x 10^{-7} sec when $r_0=0.5$ μ and when the coefficient of thermal conductivity of PE biological tissue is $\chi=1.73 \times 10^{-3}$ cm^2/sec [5]. For short pulses for which $t_i>t_1$, heat exchange between the granule and the environment is practically absent during the

time of the pulse's action, which is confirmed by direct numerical calculations and analysis of the solution [8]. Consequently the condition of uniformity of temperature T_g throughout the granule volume is fulfilled. In the case of pulses with $t_u > t_r$, the approximation of the granule's quasi-stationary heat exchange with the environment is valid, and temperature T_g is the average temperature for the granule's volume. With regard for (6), (7) and the relationship of k to T, equation (5) has an analytical solution describing heating of a granule by radiation when I_u=const for two values of α:

$$\alpha=0:\ T_g=T_\infty+\frac{I_u K_v r_g}{4k_\infty}\left[1-\exp(-Bt)\right], \qquad (8)$$

$$\alpha=1:\ T_g=T_\infty A\frac{A+1-(A-1)\exp(-BAt)}{A+1+(A-1)\exp(-BAt)},$$

where

$$A=\left(\frac{I_u K_v r_g}{2k_\infty T_\infty}+1\right)^{1/2},\quad B=\frac{3k_\infty}{\rho_g C_g r_g^2}.$$

Assuming that by the end of the radiation pulse's action when $t=t_u$ a certain critical temperature T_c is reached, and an expression can be found from (8) for the threshold intensity of radiation I_u. For example when $\alpha=0$

$$I_u(I_g)=\frac{4k_\infty(T_g-T_\infty)}{K_v r_g\left[1-\exp(-Bt_u)\right]}. \qquad (9)$$

When the condition $Bt_u<1$, which is equivalent to the condition $t_u<t_r$, is satisfied, such that removal of heat from the granule by thermal conductivity could be ignored over time t_u when $\alpha=0$ we get the following from (8) and (9) upon expanding the exponent:

$$T_g=T_\infty+\frac{3I_u(I_g)t_u K_v}{4\rho_g C_g r_g},$$
$$I_u(I_g)=\frac{4\rho_g C_g r_g(T_g-T_\infty)}{3K_v t_u}. \qquad (10)$$

Heating of nonpigmented biological tissue may be estimated without regard for heat exchange using the formula

$$T=T_\infty+\frac{\alpha_v I_u t_u}{\rho C}, \qquad (11)$$

which follows from the equation for heating of matter $\rho C(dT/dt)=\alpha_v I$ disregarding heat loss, where α_v—coefficient of absorption of biological tissue; ρ, C—density and heat capacity of biological tissue. Considering that in the pigmented layer $\alpha_v=\pi N_g r_g^2 K_v$, given identical parameters of radiation I_u, t_u and of biological tissue and granules $\rho=\rho_g$, $C=C_g$, we get the following from (10) and (11):

$$T-T_\infty=(T_g-T_\infty)K_v, \qquad (12)$$

where $K_v=(4/3)\pi N_g r_g^3$—coefficient of volume filling, defined as the proportion of the volume occupied by granules in a unit volume of biological tissue; N_g—concentration of granules. The value $K_v=0.15$ was used in the calculations below.

Relationship (12) shows that at a fixed value of laser pulse energy, heating of the entire volume of biological tissue $T-T_\infty$ will be lower than heating of granules T_g-T_∞ by as many times as the volume occupied by the granules is smaller than the total volume of the biological tissue. On the other hand when the volume of biological tissue is heated to a certain threshold temperature, $1/K_v$ times more energy must be expended than when heating granules to the same temperature in the case of selective absorption of radiation energy, which proportionately decreases threshold energies evoking the start of processes on the granules.

As was noted earlier, attainment of a certain granule temperature as a result of the action of a radiation pulse may cause initiation of a physicochemical process, the results of the action of which are determined after the end of the laser pulse, and which manifest themselves in the state of the biological tissue (coagulated biological tissue, rupture of vessels, hemorrhaging, mechanical damage to biological tissue and pigmented granules, etc.).

As the results of direct numerical calculations show, selective thermal denaturation of pigmented granules occurs when they are heated by short radiation pulses in the 1 nsec<t_u>1 μsec duration interval to a temperature T_c approximately equals350-360 K, and in the 1 μsec<t_u>1 msec interval to T_c approximately equals 420-440 K [7,8]. The difference in threshold temperatures for different t_u is explained by the fact that the rate of thermal denaturation depends strongly on temperature, and the reaction proceeds over a characteristic time on the order of the pulse duration—that is, the shorter the pulse, the higher must be the granule heating temperature resulting in thermal denaturation of more than 50

percent of the protein molecules within the granule volume.

Figure 2 gives values of radiation pulse energy Q_{λ} calculated numerically [10] and analytically with formulas (9), (4) using the cited $T_g=T_{cr}$ and leading to granular thermal denaturation in the rabbit PE (in application to the following experimental conditions [12]: λ=1.06 μ, $R_0(X_0)$=50 μ, r_g=1 μ). The figure also gives experimental values of Q_{λ} evoking ophthalmoscopically observable damage on the retina with probability on the order of 0.1 percent. Satisfactory agreement between experimental and theoretical energy values for t_i<10 μsec is noted. When t_i approximately equals 10^{-3} sec, the analytically calculated energies Q_{λ} exceed experimental and numerically calculated [10,11] values. The difference is due to disregard for the increase in temperature of surrounding biological tissue during heating and intensive heat exchange of granules with the environment in the analytical examination, and the fact that it is accounted for in the numerical solution. The results of similar analytical and numerical [10,11] calculations of Q_{λ} for the experimental conditions in [13] (λ=1.06 μ, $R_0(X_0)$=40 μ when r_g=1 μ) are shown in Figure 3 for the case of the action of radiation on the retina of a monkey eye.

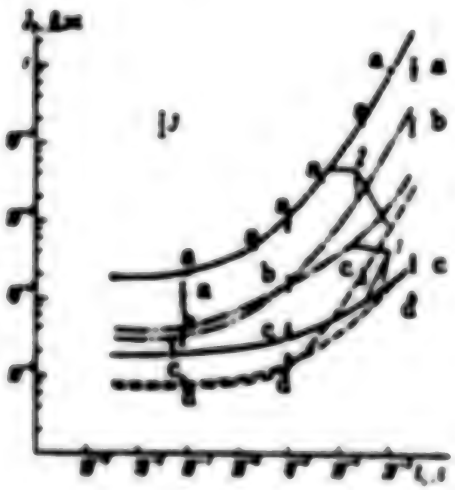


Figure 2.

Relationship of Numerically (1) and Analytically (2) Calculated Energies: Q_{λ} (broken curve), Q_{∞} (continuous), Q_{∞} (dot-dash) and Q_{cr} (curve with crosses) of Radiation Pulses With λ=1.06 μ Acting on the Cornea of a Rabbit Eye, Where the Diameter of the Irradiation Spot on the Retina is D_0=100 μ, to t_i: Experimental values are presented for laser pulse energies [12]: points Δ and o correspond to densities causing an ophthalmoscopically observable focus of damage on the retina with probabilities of 0.1 and 50 percent; points solid circle and x correspond to energies causing subretinal and preretinal hemorrhaging in tissues of the ocular fundus. The experimental value (3) of energy [13] leading to water breakdown is also given.

Key: —1. joules; —2. sec —a.= x; –b. = solid circle; –c. =o; –d. = Δ

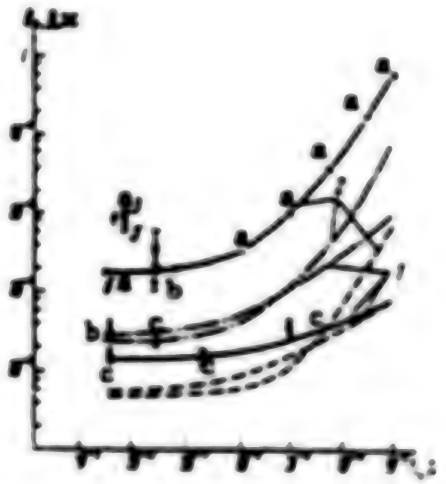


Figure 3.

Relationship of Numerically (1) and Analytically (2) Calculated Energies Q_{λ} (broken curve), Q_{∞} (continuous), Q_{∞} (dot-dash) and Q_{cr} (curve with crosses) of Radiation Pulses With λ=1.06 μ Acting on the Cornea of a Monkey Eye, Where the Diameter of the Irradiation Spot on the Retina is D_0=80 μ, to t_i: Experimental values are presented for laser pulse energies [14,15]: points o correspond to densities causing an ophthalmoscopically observable focus of damage on the retina with probabilities of 50 percent; points solid circle and x correspond to energies causing subretinal and preretinal hemorrhaging in tissues of the ocular fundus. Experimental values (x) are given for energies [16] leading to optical breakdown of distilled water (3), saline solution (4), a calf's vitreous body (5) and industrial water (6).

Key: —1. joules; —2. sec —a.= x; –b. = solid circle; –c. =o

The results of analytical estimates and direct numerical calculations show that explosive boiling of water in water-containing biological tissue adjacent to the surface of a granule heated by radiation occurs when the granule volume is heated to a threshold temperature T_{∞} approximately equals 900 K. Presence of intensive heat exchange in the surface layer of the granule has the consequence that the temperature of the surface of the granule and of water layers adjacent to it is 580-590

K in this case—that is, it corresponds to the temperature of explosive boiling (intensive homogeneous steaming) of water [17]. Figures 2 and 3 give the results of numerical [10,11] and analytical (with $T_c=T_{cr}=900$ K) values of energy Q_{cr} leading to explosive boiling of water and formation of a steam envelope on the granule, calculated in application to the experimental conditions in [12,15]. The figures also give values of the energies [12,15] evoking experimentally recorded formation of steam bubbles in biological tissues, mechanical destruction of tissues, and subretinal hemorrhaging (bleeding in the region $X>X_2$; see Figure 1). It follows from figures 2 and 3 that analytically calculated Q_{cr} satisfactorily agree with both numerically calculated and experimentally found values. It may be concluded from such consistency that formation of gas bubbles as a result of the action of short pulses of laser radiation with energies Q_{cr} may result in subretinal hemorrhaging in tissues of the ocular fundus—that is, we can associate the physical process of explosive steam formation on granules with specific results of pulse action.

Analysis of experimental data on optical breakdown of different biological tissues and water by laser radiation pulses [2,13,16,18] permits the conclusion that the characteristic threshold temperature for the beginning of optical breakdown and plasma formation in water-containing biological tissues is T_c approximately equals 5×10^3 K. Figures 2 and 3 give the results of analytical calculation of pulse energy Q_c, measured at the cornea and causing heating of a granule for which $r_0=1$ μ located at point $X=X_2$, $R=0$ to a temperature $T_c=5 \times 10^3$ K—that is, to the start of breakdown in plasma formation, calculated for the conditions of experiments in [12,15]. They also give experimental values of pulse energies leading to preretinal hemorrhaging (diffuse bleeding in the preretinal region $X<X_2$; see Figure 1). Numerical calculations were not carried out for the complete equation system for the case of optical breakdown. Comparison of analytical Q_c and experimental Q_c energy values in figures 2, 3 shows that there is satisfactory agreement, and it provides the grounds for concluding that optical breakdown and plasma formation may lead to preretinal hemorrhaging in tissues of the ocular fundus. Note that use of T_c approximately equals 1×10^4 K, which is also used in the estimates, as the threshold temperature for the start of optical breakdown causes the values of Q_c to double, and does practically nothing to worsen agreement with experimental data. It should be pointed out that the calculated energies Q_{cr}, Q_{cr}, Q_c are only the least values (the lower limit) of energies evoking the start of the corresponding physicochemical processes, while in real conditions these processes will begin at pulse energies greater than the calculated Q_{cr}, Q_{cr}, Q_c.

Figures 2 and 3 give experimental values of the energy of laser pulses with a wavelength of 1.06 μ leading to optical breakdown of tap water when the diameter of the irradiation spot is $D_0=2R_0=100$ +/- 20 μ, $t_c=30$ +/- 5 nsec [13], and of distilled water, saline solution, the calf's vitreous body and industrial water when $D_0=75$ μ, $t_c=7$ nsec [16]. In this case the threshold energy values in [13,16] exceed the threshold energy values calculated here. This is explained by the fact that in the author's opinion the main mechanism of optical breakdown of the media studied in [16] is development of an electron avalanche, and not breakdown on absorbing granules (inclusions), which requires higher values of radiation energy.

Bleeding was observed in [19] in response to the action of single radiation pulses with a wavelength of 0.532 μ and a duration of $t_c=60$ nsec on the rabbit retina, where the irradiation spot diameter was $D_0=50$ μ and the pulse energy was $Q_c=30$ mJ. Estimation of heating of a granule for which $r_0=0.5$ and 1 μ in the experimental conditions of [19], and for a short pulse with $t_c=60$ nsec, which can be done with formula (10) without regard for heat exchange, gives an identical temperature value of $T_0=4.4 \times 10^3$ K, which is close to the breakdown threshold T_{cr} we used. Even more-significant bleeding was observed in [19] with pulse energy values of $Q_c=80$ and 100 μJ.

Bleeding was experimentally observed in [20] in response to the action of a radiation pulse from a ruby laser with a wavelength of 0.69 μ, a pulse duration of 20 nsec and a pulse energy of 50 μJ, when the diameter of the irradiation spot on the retina was 35 μ. In this case estimation of the heating of granules for which $r_0=0.5$ and 1 μ using formula (10) gives a temperature value of $T_0=5.4 \times 10^3$ K, which could have led to breakdown on the granule, and bleeding.

Besides considering the effect of laser radiation pulses on the retina, there is considerable scientific and practical interest in investigating the action of pulses on the anterior division of the eye. It was noted in [2,18] that in the presence of glaucoma in adult patients, in the overwhelming majority of cases the biological tissues of the anterior division of the eye (the angle of the anterior chamber) contains pigmented granules that play the role of absorbent inclusions when exposed to laser radiation, which facilitates breakdown and destruction (perforation) of tissue structures at characteristic intensity values of 10^8-10^9 W/cm^2. Estimation of heating of a granule for which $r_0=1$ μ under the conditions in [2] when $I=10^8$ W/cm^2 using formula (10) produces a value of $T_0=6.9 \times 10^3$ K, which corresponds to experimental optical breakdown. However, in contrast to the adult eye there are practically no pigmented granules in the angle

of the anterior chamber of a child's eye in the presence of buphthalmia. Because of this, the intensity of the acting radiation has to be raised for a positive result to occur. Buphthalmia in children was treated in [18] with a spot diameter of D_s=100 μ, duration t_s=30 nsec, pulse energies of 0.15-0.5 J, and intensity I=6 x 10^{10}-2 x 10^{11} W/cm^2. In this case microexplosions, bubble formation and other phenomena were documented experimentally. These intensity values are significantly higher than those cited for pigmented biological tissues, and they are explained by the absence of pigment granules, and by possible breakdown of homogeneous biological tissues through formation of an electron avalanche.

Thus a simple analytical model of heating of a spherical absorbent granule by a laser radiation pulse is developed in this article, making it possible to estimate the threshold energies and intensities of radiation pulses heating the granule to certain temperatures. Heating of the granule volume (or surface) to a certain temperature may initiate processes such as heat-denaturation within the granule, explosive steam formation in water-containing biological tissues, optical breakdown and plasma formation. The model also permits estimation of the heating of melanoprotein and other granules and particles in particular experimental conditions, and of the possibility of occurrence of a particular physicochemical process determining the end results (coagulation, sub- or preretinal bleeding) of the action of radiation on biological tissue. Comparison of the results of calculations with different experimental data and the satisfactory agreement indicate sufficient accuracy and reliability of the model, and of the results obtained on its basis.

Bibliography

1. Steiner, R. F. and Puliafito, C. A., "The Nd-YAG Laser in Ophthalmology," Philadelphia, Saunders, 1985.

2. Akopyan, V. S., Dantsleyko, Yu. K., Naumidi, L. P. and Prokhorov, A. M., KVANT. ELEKTRONIKA, Vol 14, 1987, p 1291.

3. Birngruber, R., Hillenkamp, F. and Gabel, V. P., HEALTH PHYS., Vol 48, 1985, p 781.

4. Pustovalov, V. K., LASER PHYS., Vol 2, 1992, p 358.

5. White, T. I., Mainster, M. A., Tips, I. H. and Wilson, P. W., BULL. MATH. BIOPHYS., Vol 32, 1970, p 315.

6. Pustovalov, V. K. and Bobuchenko, D. S., DAN BSSR, Vol 30, 1986, p 513.

7. Pustovalov, V. K. and Khorunzhii, I. A., INT. J HEAT MASS TRANSFER, Vol 30, 1990, p 771.

8. Pustovalov, V. K. and Khorunzhiy, I. A., KVANT. ELEKTRONIKA, Vol 13, 1986, p 1461.

9. Pustovalov, V. K., Khorunzhiy, I. A. and Bobuchenko, D. S., IZV. AN SSSR. SER. FIZ., Vol 52, No 9, 1988, p 1847.

10. Pustovalov, V. K. and Khorunzhiy, I. A., MAT. MODELIROVANIYE, Vol 1, No 9, 1989, p 21.

11. Pustovalov, V. K., INT. J. HEAT MASS TRANSFER, Vol 36, 1993, p 391.

12. Avdeyev, P. S., Berezin, Yu. D., Volkov, V. V. et al., VESTN. OFTALMOLOGII, No 1, 1982, p 26.

13. Pozhidayev, V. N. and Fatiyevskiy, A. I., KVANT. ELEKTRONIKA, Vol 8, 1981, p 119.

14. Allen, R. G., Thomas, S. J., Harrison, R. F. et al., HEALTH PHYS., Vol 49, 1985, p 685.

15. Blankenstein, H. F., Zuclich, J. A., Allen, R. G. et al., INVEST. OPHTHALMOL., Vol 27, 1986, p 1176.

16. Sacchi, C. A., J. OPT. SOC. AMER. B., Vol 8, 1991, p 337.

17. Skrinov, V. P., "Metastabilnaya zhidkost" [Metastable Liquid], Moscow, Nauka, 1972.

18. Akonyan, V. S., Voyebodin, Yu. G., Yegorov, Ye. I., Krasnov, M. M. et al., IZV. AN SSSR. SER FIZ., Vol 46, No 10, 1982, p 2000.

19. Mosier, M. A., Champion, J., Liaw, L. H. and Berns, M. W., LASERS SURG. MED., Vol 5, 1985, p 377.

20. Birngruber, R., Puliafito, C. A. et al., IEEE J. QUANT. ELECTRON., Vol QE-23, 1987, p 1836.

Russia: Polarization Characteristics of Radiation Scattered by the Human Integument

964D0760B Moscow IZVESTIYA AKADEMII NAUK SERIYA FIZICHESKAYA in Russian Jun 95 Vol 59 No 6, pp 84-89

[Article by L. V. Tanin, S. K. Dik and S. A. Aleksandrov, Physics Institute of the Belarusian Academy of Sciences, and Institute of Neurology, Neurosurgery and Physiotherapy of the Belarusian Ministry of Health; UDC 535.5]

[FBIS Translated Text] **Polarization characteristics of the human integument are investigated** *in vivo*. Data are compared with the results of research on a two-layer scatterer used as a physical object modeling optic properties of integument.

Contactless methods of studying biomedical objects are based on analyzing the parameters of radiation

scattered by these objects. One of the most important parameters bearing information on the structure and physical properties of the object under investigation is the state of its polarization.

The paper [1], which is devoted to interaction of linearly polarized radiation with the substance of a living leaf and to the angular and polarization structure of scattered radiation, was one of the first in this field. The degree of polarization of laser radiation with wavelengths of 1.15, 0.84, 0.63, 0.503 and 0.337 μ reflected from different organs of the abdominal cavity of experimental animals was investigated experimentally in [2]. It was established that the degree of polarization of radiation reflected from biological tissue varies for all investigated wavelengths depending on the angle of incidence and the radiation's polarization.

The goal of our work was to investigate the polarization characteristics of human integument *in vivo* under normal conditions and in the presence of pathology (artificially evoked ischemia). The ability of certain models used to describe the characteristics of a light field scattered from black [3] and transparent glass with one frosted edge [4] to explain polarization properties of human integument was studied. In addition research was conducted on a modeled object of more-complex structure—a two-layer scatterer. An object of this kind corresponds to a greater degree in its light-scattering characteristics to integument than do the objects of research in [3,4], inasmuch as skin is a multilayered structure [5]. The structure of the speckle field formed by light scattered from such an object was investigated in [5], but its polarization properties were not studied.

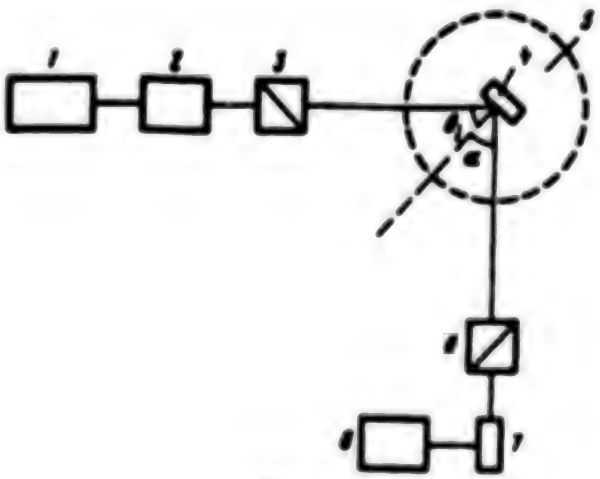


Figure 1.

An experimental device diagrammed in Figure 1 was assembled for the research. An He-Ne laser was used as the light source. Linearly polarized radiation passed through a crystalline $\lambda/4$ plate 2 oriented diagonally. Circularly polarized radiation then struck a polarizer 3, which isolated the needed direction of oscillations and then illuminated the object under investigation 4, mounted near the axis of rotation of a goniometer 5. A special support for the right index finger was secured to the goniometer. To avoid possible random vibrations the subject's forearm was rigidly secured. The direction of the plane of oscillations of radiation after the polarizer 3 was an angle ϕ=45° to the plane of incidence. In this case the intensity of the two mutually perpendicular components of the light wave are equal, and consequently change in the wave's polarization as a result of interaction with the surface in question makes it possible to assess the degree of polarization of natural light.

Polarization of the radiation changes when it is scattered by the object under investigation 4. Scattered radiation passing through analyzer 6 is recorded by a photomultiplier 7 and a voltmeter 8. When analyzer 6 is set for passage of light oscillations with azimuths 0, $\pi/2$, ϕ, ϕ +/- $\pi/2$, we can determine the change experienced by a beam of both natural and linearly polarized radiation upon its reflection [3].

The value we get from the first two readings N_0 and $N_{\pi/2}$ for the degree of polarization of natural radiation upon reflection is

$$P = \frac{N_0 - N_{\pi/2}}{N_0 + N_{\pi/2}}. \qquad (1)$$

The plane of oscillations of the electric vector in the reflected beam is found to be turned by some angle ϕ compared to that in the incident beam, measured experimentally by a scale applied to the frame of the analyzer, and it corresponds to the reading N_ϕ—that is, to the maximum intensity of reflected radiation.

Had the reflected beam remained completely linearly polarized, reading $N_{\phi \pm \pi/2}$ would have been zero. But because the beam partially depolarizes upon reflection, this reading is not equal to zero, and the degree of the beam's depolarization may be calculated by the expression

$$A = 1 - P_1 = 1 - \frac{N_\phi - N_{\phi \pm \pi/2}}{N_\phi + N_{\phi \pm \pi/2}}. \qquad (2)$$

P_1 and Δ characterize the change experienced by beams of natural and linearly polarized radiation, although in both cases the incident beam is completely linearly polarized [3].

Investigation of biomedical objects *in vivo* is associated with certain difficulties. The optical properties of the same object can be different in different points of it, and they may vary over time even if external conditions are kept constant with the best possible precision. Therefore when studying a living organism using state-of-the-art equipment of a physical experiment, it is fundamentally impossible to reach the same reproducibility of data that is achieved with a purely physical object. All measurements were taken several times and subjected to statistical treatment.

Investigation of the degree of polarization of natural light P_1 as a function of the angle of observation permits the conclusion that when α is below -70° and above 50°, P_1 depends significantly on the incidence angle. The maximum degree of polarization is 14 percent. Relative measurement error did not exceed 2 percent. In the range of angles α from -70 to 40°, the degree of polarization of natural radiation scattered by the human integument does not exceed 1 percent.

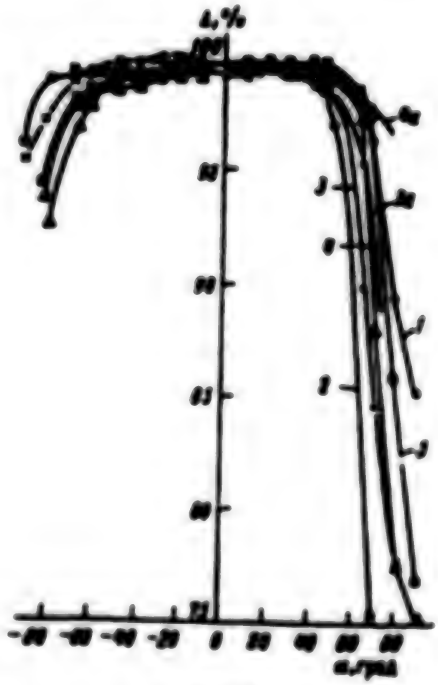


Figure 2

Figure 2 shows graphs of the relationship of depolarization of linearly polarized radiation scattered by the inside surface of the human right index finger to observation angles α for different angles of incidence θ_1. The numbers on the curves of all graphs correspond to the following incidence angles: 1—0; 2—10; 3—30; 4—50; 5—70°.

Depolarization of linearly polarized radiation increases for angles from -90 to -20°, and remains constant for angles of observation from -20 to 30°. After >a=30°, the curves begin to drop off gently, while abrupt reduction of depolarization is noted at α=50°. The relationship of depolarization of radiation to angle of incidence can be seen in Figure 2 at observation angles from 50 to 90°: As the angle of incidence grows, the degree of polarization rises. The curve for which θ_1=0 is an exception. A high degree of depolarization, on the order of 90 percent, is observed at angles α from -50 to 40°—that is, linearly polarized radiation is practically completely depolarized upon reflection from integument.

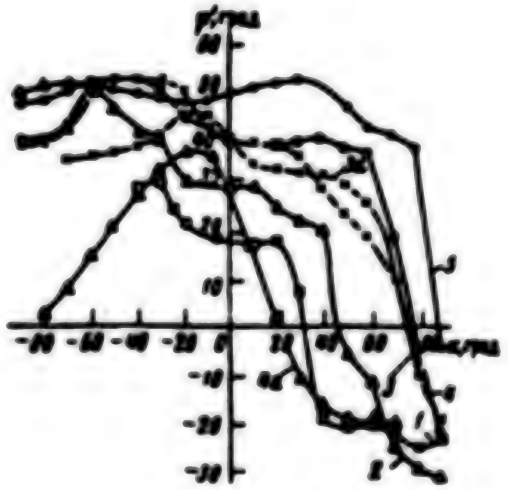


Figure 3

Figure 3 shows the relationships of the angles of rotation of the polarization plane to the angles of observation. At observation angles from 5 to 65°, the azimuth angles of rotation of the polarization plane are found to depend on the angles of incidence: The angle of rotation decreases as the angle of incidence increases. Relative measurement error did not exceed 15 percent.

In order to study the influence of change in functional state of the human body on the polarization characteristics of radiation scattered by the human integument, these characteristics were investigated in the presence of artificially induced ischemia. Prior to the start of the experiment an inflatable cuff was placed over the subject's arm, and ischemia was caused by inflating it with air.

Angles of incidence θ_i=30 and 50° were then measured according to the procedure described above. The degree of polarization of natural light at an incidence angle of θ_i=30° grew within the range of observation angles α=20-60°, where the difference between the measurement results with and without compression reached 4 percent. It did not exceed 1 percent for an incidence angle of θ_i=50°.

Changes in depolarization of linearly polarized light are also most noticeable at an incidence angle of θ_i=30°. Quantitative differences between depolarization in normal state and in the presence of compression (curves 3 and 3a in Figure 2) increase with growth of the angle of observation, and at α=70° the difference is 6 percent. As far as the relationship of the azimuth angles of rotation of the polarization plane to the angle of observation is concerned, differences between the trend of the curves in normal conditions and in the presence of ischemia (Figure 3) are not large, and they permit us to reach reliable conclusions regarding presence or absence of a pathological state.

The setup used to study radiation scattered by a glass plate with two frosted surfaces is similar to that described for research on the human integument *in vivo*, except for certain changes associated with installing a plate holder in place of the special support for the right index finger. The same four parameters of radiation scattered by the frosted surfaces of the plate were recorded—N_p, $N_{\perp p}$, N_c, $N_{c \perp c p}$. The degree of polarization of natural light P_i depends to a significant degree on the incidence angle θ_i, and in the range of observation angles from 0 to 80° it increases for θ_i=0, 10, 30°, which corresponds to the results in [3]. For θ_i=50 and 70°, the values of P_i decrease on the average in the same range, which is more consistent with the results in [4] for light passing through a glass plate with one frosted surface. Maximum polarization of natural radiation is 46 percent.

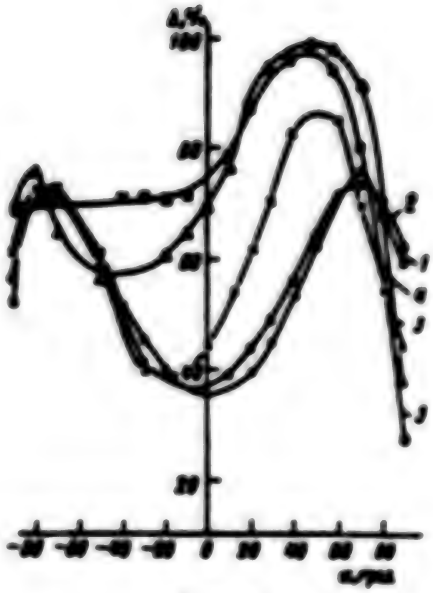


Figure 4

Figure 4 shows graphs of the relationship of the degree of depolarization of linearly polarized radiation to the angle of observation. The numbers on the curves of all graphs correspond to the following incidence angles: 1—10; 2—10; 3—30; 4—50; 5—70°. Local maximums of experimental curves are noted at observation angles α within the 35-75° interval, with the degree of depolarization growing as the angle of incidence increases. Local minimums observed at angles α from 0 to -50° shift with increasing incidence angle in the direction of smaller values of the angles of observation. Maximum depolarization is 97 percent. Measurement error did not exceed 2 percent.

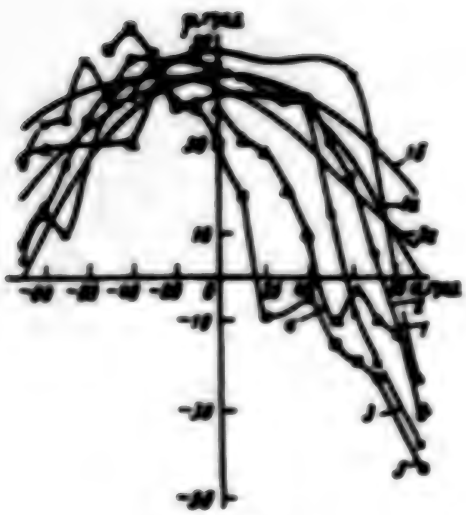


Figure 5

Comparison of the results in Figure 4 and in [3] showed that for incidence angles θ_0>45° and observation angles α>50°, a decrease in the degree of polarization is typical of both cases. For angles θ_0<45° and α from 0 to 60°, the degrees of depolarization increase, which is consistent with data in [4]. Comparison of data obtained in [3,4] with those in Figure 4 permitted the conclusion that the latter are closer to the results described in [4].

Figure 5 gives curves for rotation of the plane of polarization of scattered radiation as a function of the angle of observation, and it provides the corresponding theoretical curves. Curves 1b and 3a were calculated using a formula from [3]:

$$\operatorname{tg}\phi' = -\frac{\cos\left(\frac{\alpha+\theta_0}{2}-\mu\right)}{\cos\left(\frac{\alpha+\theta_0}{2}+\mu\right)}\operatorname{tg}\phi, \qquad (3)$$

where μ—angle of refraction determined by Snellius's invariant:

$$\sin\frac{\alpha+\theta_0}{2} = n\sin\mu, \; n = 1.52$$

respectively for θ_0=0 and 30°, with regard for a shift angle of $\pi/2$ for the oscillation plane.

Curve 1a was calculated using a formula from [4]:

$$\operatorname{tg}\phi' = \operatorname{tg}\phi\cos\alpha. \qquad (4)$$

It is evident from Figure 5 that in the range of observation angles from -55 to 75°, theoretical curve 1b agrees better with experimental curve 1. The error averages 7 percent. Theoretical curve 3a for θ_0=30° coincides satisfactorily with experimental curve 3 in the range of angles from -90 to 50°. When α>50°, the experimental value of ϕ' decreases much faster than the theoretical value.

Analysis of the experimental data showed that in our case both scattering from the edges upon reflection and refraction upon passage of radiation through the substance of the glass affect the polarization properties of scattered radiation. Presence of two frosted surfaces qualitatively changes the nature of scattering. Both an external and an internal component participate in forming the scattered radiation. To create a mathematical model that describes the obtained results more adequately, we must account for polarization effects arising upon reflection from an optically denser medium during transmission [3], and for scattering upon reflection from a medium with a lower index of refraction and upon double transmission through a frosted surface [4].

The overall trend of the experimental curves characterizing the degree of polarization of natural light scattered by the human integument correlates with the corresponding curves for a two-layer scatterer when θ_0 is not equal to 50 and 70°.

Analysis of the trend of curves characterizing the degree of depolarization of linearly polarized light upon scattering by human integument (Figure 2) and upon scattering by frosted glass with two rough surfaces (Figure) shows that agreement is satisfactory when θ_0=70°.

Qualitative and quantitative agreement is observed when we compare experimental curves characterizing change in the azimuth angles of the inclination of the plane of polarization of scattered radiation in the case of a frosted plate (Figure 5) and human integument (Figure 3). Both the general trend of the curves and the dependence on angle of incidence remain consistent.

Conclusion

The research conducted on polarization characteristics of radiation scattered by a glass plate with two rough surfaces and the comparison of the results with theoretical and experimental data for mathematical models in [3,4] showed that effects inherent to both models influence the results. Adequate description of the results

requires consideration of the aggregate of processes occurring as radiation passes through the scattering layer, reflection from a scattering layer with a large index of refraction, reflection from a scattering layer with lower density, and scattering upon repeat transmission through the scattering layer.

Research on the polarization characteristics of radiation scattered by the human integument and comparison of the results with data [3,4] permitted the conclusion that the polarization characteristics of radiation scattered by the human integument *in vivo* are not described adequately by either of the considered models. The reasons for this are the complex structure of integument, scattering by its internal structures and capillaries, the influence of blood flow, and so on.

The two-layer scatterer investigated in this study was found to be closer in its polarization properties to integument than the models examined in [3,4].

The research described here on polarization characteristics of radiation scattered by the human integument in the presence of artificially induced ischemia, and a comparison of the results with the same characteristics in normal conditions showed that the greatest changes in polarization characteristics of scattered radiation occurred at an incidence angle of 30° and an observation angle of 60°.

Bibliography

1. Rvachev, V. P. and Guminetskiy, G., ZHURN. PRIKL. SPEKTROSKOPII, Vol 4, 1966, p 415.

2. Aturtekov, S. A. and Madzhidov, R. T. "Nauka prakticheskomu zdravookhraneniyu. sb. tr. nauch.-prakt. konf." [Science in Aid of Practical Public Health. Collection of Papers of a Scientific-Practical Conference], Makhachkala, 1985.

3. Rvachev, V. P. and Polyanskiy, V. K., OPTIKA I SPEKTROSKOPIYA, Vol 18, 1965, p 1057.

4. Polyanskiy, V. K. and Rvachev, V. P., OPTIKA I SPEKTROSKOPIYA, Vol 20, 1966, p 701.

5. Asakura, T., ANRITSU NEWS, Vol 8, No 38, 1988, p 9.

Russia: Use of a Mixture of the First and Second Harmonics of a Neodymium Laser for Therapeutic Photocoagulation of Tissues of the Ocular Fundus

964D0760C Moscow IZVESTIYA AKADEMII NAUK SERIYA FIZICHESKAYA in Russian Jun 95 Vol 59 No 6, pp 90-94

[Article by G. I. Zheltov, A. S. Podoltsev, A. I. Kirkovskiy, M. V. Belokon, V. N. Glazkov and L. A. Linnik; UDC 621.378.325:612.84:519.6]

[FBIS Translated Text] **A method is proposed for treating eye diseases based on the fact that under certain conditions the thermal and biological effect produced by a mixture of wavelengths λ_1 and λ_2 with a given intensity ratio is equivalent to the effect produced by monochromatic radiation in the interval from λ_1 to λ_2. The therapeutic effect and functional possibilities of such an apparatus are significantly greater compared to devices using a set of different lasers.**

Laser treatment methods open up possibilities for individually tailoring the method of approaching a specific pathology in a specific patient in the most precise way. One of the possible approaches to solving this problem in treating diseases of the ocular fundus by photocoagulation might be to use high-power lasers with adjustable radiation wavelength.

Tissues of the fundus are a complex of structural elements with different spectral coefficients of absorption. By using radiation of different spectral composition, it would be fundamentally possible to focus the radiation's effect on particular elements, and to control the shape, depth and location of zones of coagulation within wide limits with regard for tissue pigmentation [1,2].

Several types of lasers generating radiation in different spectral regions are used in ophthalmological practice. We know of attempts to combine the merits of several laser ophthalmocoagulators in a single instrument using a tunable dye laser [3-6]. The requirements on the parameters of such a laser are rather high. The minimum duration of the coagulating light pulse must be on the order of milliseconds, radiation power must be in the units of watts and higher, laser beam spread should be in the units of minutes, and the radiation wavelength tuning range should be approximately from 500 to 1,000 nm.

Creation of an ophthalmocoagulator based on a laser with the indicated parameters is not a simple technical problem, and according to our information no original approaches to solving it that would ensure commercial feasibility of manufacturing such instruments have yet been found.

The object of this communication is to describe a laser for photocoagulation of tissues of the fundus possessing possibilities which are the same as of a laser with an emission wavelength of the 530-1,060 nm range in terms of selective action upon individual elements of tissue structure and control of the spatial characteristics of the coagulation zone [7]. This development is based on equivalency of the thermal effect of radiation containing two spectral components λ_1 and λ_2 with a particular intensity ratio on tissues of the fundus to the action of monochromatic radiation with wavelength λ_3 lying within the interval λ_1-λ_2. This effect of equivalency was discovered in the course of a computer experiment using a mathematical model we developed for injury to the fundus by high-intensity optical radiation. The mathematical methods and the basic formulas used in the modeling were presented in their most general form in [8,9], and they are described qualitatively in [10]. We will limit ourselves here to a condensed description of the physical model and the adopted approximations.

To recall briefly, this is a three-dimensional model of a multilayered structure. The layers differ in spectral absorption coefficients and thermophysical parameters, with the indicated properties and thicknesses of the layers corresponding to the structure of the fundus of the human or animal eye used as the object of modeling.

The radial distribution of the intensity of radiation focused on the retina is assumed to be Gaussian. As in [10-12], it is assumed that damage to the native structure of cell proteins is thermochemical in nature. The rate constants of thermal denaturation of tissues of the human retina are assumed to be equal to the corresponding constants for the rhesus monkey, found experimentally [13].

The results of calculating the energy of radiation causing initial irreversible changes in retinal tissues correspond to data obtained in therapeutic laser photocoagulation of the retina of Europeans 20-25 years old exhibiting pronounced pigmentation of the fundus [14]. Some of the modeling results are shown in Figure 1.

The energy (power) of radiation causing irreversible damage to an area of the retina's pigmented epithelium 40 μ in diameter is conditionally adopted here as the threshold. It is assumed that approximately 70 percent of the molecules of native proteins were damaged as a result of thermal destruction on the boundary of this region.

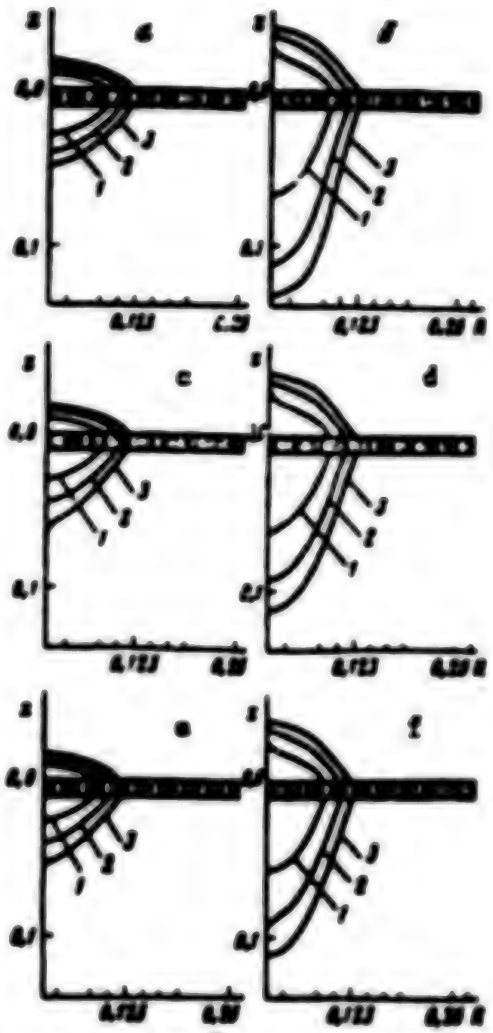


Figure 1. Calculated Boundaries of the Regions of Primary Photodestruction of Tissues of the Fundus in Coordinates R, z (mm): The contours of the regions are shown for double (1), triple (2) and quadruple (3) the threshold energy. The radius of the irradiated zone of the retina is 0.1 mm; the shaded bar is the pigmented epithelium. The spectral composition of radiation and the pulse duration are: a—λ=532 nm, τ_p=2 x 10^{-3} sec; b—λ=1,060 nm, τ_p=10^{-3}; c—λ=650 nm, τ_p=2 x 10^{-3} sec; d—λ=650 nm, τ_p=10^{-3} sec; e—a mixture of radiation with wavelength λ_1=532 nm (15 percent of the power) and λ_2=1,064 nm, τ_p=2 x 10^{-3} sec; f—a mixture of radiation with wavelength λ_1=532 nm (25 percent of the power) and λ_2=1,064 nm, τ_p=10^{-3} sec

As is evident from the figure, the action of individual components of monochromatic radiation (Figure 1, c,

d) and combinations of wavelengths of 530 and 1,060 nm corresponding to them (Figure 1, e, f) produce identical results. Similar data confirming the possibility of simulating the effect of monochromatic radiation in the 530-1,060 nm spectral interval on the fundus by a mixture of the indicated spectral components were obtained for an exposure time of 10^{-1}-10^{-2} sec and for diameters of the exposed region of the retina from 50 to 500 μ.

A mockup of an ophthalmocoagulator with a YAG laser operating in quasi-continuous mode (the radiation pulse duration is (2-5) x 10^{-3} sec) with a doubled emission frequency was developed and created for the biomedical tests. A system for doubling the OOS [not further identified] that ensures orthogonal polarization of the main frequency (1,064 nm) and the harmonic (532 nm) was employed. This made it possible to use a system of two polarizers positioned in series to control the beam's energy parameters. The position of the first polarizer determined the ratio of the intensities of the spectral components, while the second polarizer acted as a regulator of the total radiation energy. The range of radiation energy regulation at the device's output was 10^{-1}-1 and 10^{-2}-0.25 J for the main and doubled radiation frequency respectively.

The mockup of the instrument underwent two cycles of biomedical tests on animals: The first was carried out in the CIS's leading ophthalmological clinic—the Scientific Research Institute of Ocular Diseases and Tissue Therapy imeni F. P. Filatov in the city of Odessa, and the second was carried out at the Primate Center of the Institute of Experimental Pathology and Therapy in the city of Sukhumi [15]. The first cycle included ophthalmological and biomicroscopic (for the case of lengthy periods) and histopathological (for the case of periods of up to a month from the moment of exposure) research on the features of formation and development of coagulation foci on the fundus of rabbits in relation to different ratios of the intensities of the spectral components of the radiation. The second research cycle was conducted on monkeys. The same methods were used here, with the additional inclusion of direct comparison between the coagulating action of emissions of a ruby laser and a mixture of 1,064 and 532 nm spectral components of corresponding biological action under otherwise equal conditions.

This research showed (we cite the medical conclusion) that "the possibility exists for microsurgical laser treatment of central divisions of the optical fundus differentiated with respect to histological level." The architectonics of the chorioretinal commissure may vary from cone-shaped (with the base on Brukh's [transliteration] membrane and the apex in the plexiform layer) to ellipsoid, flattened in the direction of Brukh's membrane. In the latter case the retina is practically intact.

The architectonics of the chorioretinal commissure resulting from the action of a mixture of the two spectral components indicated above at a ratio of $P_{\lambda=532}/P_{\lambda=1064}=1/20$ on the ocular fundus of rhesus monkeys is close to what is obtained with a ruby laser (λ=694 nm). In both cases the pulse duration is 2 x 10^{-3} sec, and the diameter of the exposed region of the retina is approximately 150 μ.

The instrument mockup was recommended for clinical tests. Tests were conducted at the Scientific Research Institute of Ocular Diseases and Tissue Therapy imeni V. P. Filatov. Specialists gave a high assessment to the instrument and the method. It was noted to have a positive effect in the treatment of post-traumatic proliferations of the retina, ruptures of the vascular membrane and neovascular membranes, peripheral degenerations of the retina, and melanoblastomas. Special mention was made of the looser requirements on the therapeutic radiation dosage. The concluding part of the official clinical test certificate noted the following: "The proposed method and ophthalmocoagulator made it possible to treat intraocular pathology using two-color laser radiation for the first time, which provided a possibility for selective action on tissues with the purpose of producing coagulation foci differing in area and depth. Use of this method made it possible to raise the effectiveness of laser coagulation, reduced the recovery time of patients and the number of sessions of laser coagulation compared to traditional instruments, and opened up new possibilities for treating eye diseases."

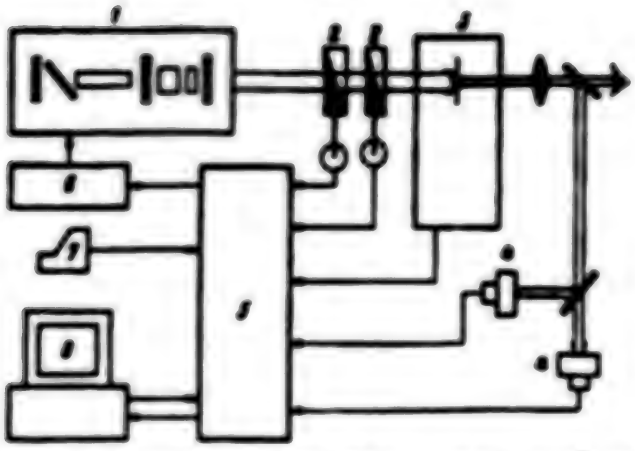


Figure 2. Structural Diagram of the Ophthalmocoagulator: —1. laser, —2. total radiation energy and spectral component intensity ratio regulator, —3. system transporting radiation energy to the operating zone, providing for adjustment of the diameter of the exposed region of the fundus, —4. photodetector, —5. microprocessor system controlling the mechanisms regulating the radiation parameters, —6. remote console, —7. personal computer

Development of an industrial model of the laser ophthalmocoagulator is presently nearing completion. Its structure is diagrammed in Figure 2. We felt it suitable to limit ourselves in this instrument to five discrete values of the ratios of spectral component intensities, to simulate the effect of lasers with wavelengths of 532, 650, 750, 850 and 1,064 nm, and to somewhat increase the total radiation energy. Our objective is to make the level of the instrument's automation and the extent to which it could be serviced by the physician correspond to the latest requirements.

The radiation parameter control system may be connected to a personal computer, for which a special package of programs carrying out several functions is being written:

1. Displaying in graphical and digital form the relationship of the shape and location of the tissue destruction zone to the parameters of the laser radiation, with regard for individual features of the irradiated object.

2. Predicting possible complications in laser surgery taking the form of hemorrhaging, formation of steam-and-gas bubbles etc. with given probability.

3. Solving the reverse problem of determining the characteristics of a laser beam needed for a particular effect.

4. Storing, processing and retrieving information in a form convenient to the physician on patients, on the types and typical features of disease, on the effectiveness of using laser treatment methods, etc.

When necessary, the physician's actions may be monitored by a computer during surgery. In this case an automatic system for blocking laser action when there is a high probability of bleeding is ensured. The computer will help the physician model the forthcoming operation and select the optimum radiation parameters for the best therapeutic effect. Obviously the program may be useful in training novice laser ophthalmic surgeons.

A large volume of calculated relationships similar to those in Figure 1 pertaining to the emission wavelength (including the simultaneous action of 532 and 1,064 nm components), pulse duration and the diameter of the exposed region of the retina is being used to write the package of programs. The threshold conditions for appearance of steam-and-gas bubbles and subretinal hemorrhaging were found on the basis of experimental data similar to those cited in [16,17]. The calculation results were tabulated. This ensures practically instantaneous reaction of the computer both when working with the user in interactive mode and when monitoring the actions of the physician.

In conclusion the authors would like to thank the physicians, engineers and scientific workers who took part in work on the instrument, and express the hope that this work will be useful to people.

This project was supported (as concerns investigation of the mechanisms of the action of laser radiation on tissue) by a grant from the Soros Fund provided by the American Physics Society.

Bibliography

1. Ham, W. T., Ruffolo, J. J., Mueller, H. A. and Du Pond, G. III, VISION RES., Vol 20, No 12, 1980, p 1105.

2. Kalinkin, A. V., Bolyunov, A. V., Ziangirova, G. T. and Fedorova, A. A., VESTN. OFTALMOLOGII, No 5, 1988, p 61.

3. Burlamacchi, P., Pratesi, R. and Vanni, V., REV. SCI. INSTRUM., Vol 66, No 3, p 281.

4. Linnik, L. A. and Repyakh, V. S., "Sredstva i metody kvantovoy elektroniki v meditsine" [Resources and Methods of Quantum Electronics in Medicine], Saratov, 1976, p 92.

5. Brancato, R., Burlamacchi, P., Pratesi, R. and Vanni, V., OPHTHALMOLIGICA, Vol 171, No 2, 1975, p 146.

6. Bass, H. S., Perkins, E. S. and Wheeler, C. B., ADV. OPHTHALM., Vol 34, 1977, p 164.

7. Gutlin, Ye. M., Glazkov, V. N., Zheltov, G. I., Linnik, L. A., Meshkov, G. G., Podoltsev, A. S., Privalov, A. P., Repyakh, V. S. and Tverskoy, Yu. L., USSR Author's Certificate 1292221 (Priority as of 19 April 1983).

8. Zheltov, G., Glazkov, V., Kirkovsky, A. and Podoltsev, A., LASERS LIFE SCI., Vol 4, No 3, 1991, p 135.

9. Zheltov, G. I., Glazkov, V. N., Linnik, L. A. et al., KVANTOVAYA ELEKTRON., Vol 10, No 8, 1983, p 1684.

10. Barns, F. S., "Laser Appl. Med. Biol.," 1974, p 205.

11. Bringruber, R., Hillenkamp, F. and Gabel V. P., HEALTH PHYS., Vol 48, No 6, 1985, p 781.

12. Hayes, J. R. and Wolbarsht, M. L., "Laser Appl. Med. Biol.," 1971, p 255.

13. Gapeyeva, T. A., Glazkov, V. N., Podoltsev, A. S., Zheltov, G. I. and Meshkov, G. G., VESTSI AN BSSR. SER. FIZ.-MAT. NAUK, No 3, 1986, p 81.

14. Linnik, L. A., Zheltov, G. I., Glazkov, V. N. et al., OFTALMOLOGICHESKIY ZHURN., No 6, 1988, p 335.

15. Ivanishko, Yu. A., Zheltov, G. I., Goryun, G. G., Linnik, L. A. and Privalov, A. P., "Tez. dokl. V vsesoyuz. konf. 'Optika lazerov'" [Abstracts of Reports of the 5th All-Union Conference "Laser Optics"], Leningrad, 1986, p 326.

16. Bringruber, R., "Laser in der Ophthalmologie," Stuttgart, Ferdinand Enke Verlag, 1988, p 31.

17. Wolbarsht, M. L. and Allen, R., APPL. OPT., Vol 25, No 10, 1986, p 1533.

Russia: Study of Effect of Associative Optical Memory in Multilayer Structures Based on Electro-Optical Crystals

964D0763 Moscow IZVESTIYA AKADEMII NAUK. SERIYA FIZICHESKAYA in Russian Jun 95 Vol 59 No 6, pp 42-48

[Article by A.A. Berezhnoy and T.N. Sherstneva, All-Russian Science Center, State Optical Institute imeni S.I. Vavilova; UDC 535.241.13:537.228]

[FBIS Summary] The electro-optical properties of ferroelectric crystals can be related to a model of a neuron lattice capable of sensing the specific interaction of local fields as a function of the character of the incoming image presented on a photoactive light carrier. The character of the reducible image depends on the correlation radius between the interacting polar fields. The implementation of associative memory depends on the number of images which can be recorded in latent form. Tests were conducted on associative optical memory based on the electro-optical effect of ferroelectric crystals of lead magnesium niobate $PbMg_{1/3}Nb_{2/3}O_3$ (PMN), strontium-barium niobate $Ba_{0.4}Sr_{0.6}Nb_2O_6$ (NBS), and lead germanate $Pb_5Ge_3O_{11}$ (PGO). These crystals were selected because they have a latent optical memory, and there is substantial nonlocality of the interaction of the dipole moments of spontaneously polarized microfields. These crystals can keep recorded information in latent form. Loss of contrast was considerable for all crystals studied, a disadvantage, although latent form storage was greater by several orders of magnitude. Electro-optical hysteresis in PMN and NBS crystals is depicted graphically. PMN is a multiaxial ferroelectric, and NBS is monoaxial. The difference in the curves for PMN and NBS crystals consists in the presence of a critical field for NBS crystals, within which an increase in the field and a drop in double refraction is observed. This indicates that the orientation of spontaneous polarization is possible in the direction of the field not coinciding with the direction of the ferromagnetic axis, an important experimental result. Figures 4; references 9: 8 Russian, 1 Western.

Russia: Radionuclide Excretion From the Bodies of Animals and Humans

964D0758A Moscow MEDITSINSKAYA RADIOLOGIYA I RADIATSIONNAYA BEZOPASNOST in Russian Vol 40 No 4, Jul-Aug 95 pp 61-66

[Article by A.S. Arkhipov and T.F. Sidorova, Biotechnologiya Scientific-Production Association; first three

paragraphs are MEDITSINSKAYA RADIOLOGIYA I RADIATSIONNAYA BEZOPASNOST abstract]

[FBIS Translated Text] The problem of excretion of radionuclides from the bodies of animals and humans is discussed in a concise historical review, and methodological approaches to the problem are considered. The results of studies of radionuclide excretion that were conducted by using chemicals and biologically active materials are presented. The review focuses on removing those radioactive elements that pose the greatest threat from the standpoint of intoxication of the organism in connection with an accident at a nuclear power plant, namely, ^{131}I, ^{89}Sr and ^{90}Sr, ^{137}Cs, ^{239}Pu, and ^{241}Am.

The results of studies of the excretion of radionuclides from humans and animals based on the dilution effect, ionic antagonism, and the use of complex-forming agents are considered. The effectiveness of using edible fibers and other sorbents, foodstuffs, and beverages is demonstrated.

It is noted that despite the progress that has been made, problems related to excretion of radioactive materials from the respiratory tract and the search for more effective preparations for removing radioactive strontium still remain unresolved.

The problem of excretion of radioactive materials from the body arose soon after the beginning of research on natural radioactive elements. The first syndromes associated with poisoning by radioactive elements were described in 1929 by Martland and Humphries.[1] Attempts to eliminate radionuclides from the body began virtually simultaneously. ^{226}Ra and other natural osteotropic radioactive elements were discussed. The first principle used in efforts to eliminate radionuclides from the body was that of attempting to alter metabolism in osseous tissue so as to "demineralize" it and thereby mobilize radioactive matter that had been deposited in the bones.

After the discovery of artificial radioactivity, especially after the use of nuclear weapons in Japan, the significance of the problem increased sharply. The biggest advance of the day was Schubert's proposal that zirconium citrate be used to accelerate excretion of radioactive Na and Pu from the body.[2] He believed that zirconium displaces radioactive metals and suggested that zirconium citrate's effect is a manifestation of the dilution effect. The use of zirconium citrate served as the foundation for a new principle—dilution of radioactive metals.

A new era began after the use of complex-forming agents, specifically, ethylenediaminetetraacetic acid [EDTA]. Virtually simultaneously, different authors reported EDTA having a significant effect on excretion of Pu and Ca from the body. Further progress was made when diethyleneaminetriaminepentaacetic acid [DTPA] was used. It was not possible to synthesize effective complex-forming agents for all radionuclides, however. Furthermore, a number of complex-forming agents turned out to be toxic, and their long-term use caused kidney damage. Consequently, the search for new chemical compounds and biologically active materials facilitating the excretion of radionuclides posing a threat to human health remains as urgent as ever. In fact, it has become even more important in view of the accident at the Chernobyl Nuclear Power Plant. The Chernobyl accident renewed world interest in the long-term consequences of internal irradiation by radionuclides as a result of contamination of the environment by radioactive fallout.

All methods of radionuclide excretion may be subdivided into two large groups. The first includes methods of removing radionuclides from primary depots: mechanical (rinsing, gastric and pulmonary lavage, enemas, etc.); physiologic (stimulating secretion of the mucous membranes of the bronchi and ciliated epithelium, inducing vomiting); and chemical bonding of radionuclides with complex-forming agents, adsorbents, and ion-exchange resins. The second group includes methods of eliminating resorbed radionuclides: isotope dissolution, ion antagonism, alteration of metabolic processes, stimulation of metabolism of natural elements of the body that are chemically similar to radionuclides, stimulation of urination, and use of complex-forming agents and adsorbents.

This review primarily considers the results of studies of using chemical preparations and biologically active materials to remove radionuclides. Studies of the removal of those radionuclides that represent the greatest threat upon intoxication of the organism will be discussed in greatest detail.

Radionuclides of iodine form in the greatest quantities upon the fission of ^{235}U, ^{238}U, and ^{239}Pu. From a toxicity standpoint, ^{131}I and ^{132}I are most interesting. Under certain conditions, however, short-lived iodine nuclides such as ^{135}I, ^{134}I, and ^{133}I may be the biggest contributors to the overall toxic effect. Upon entering the body, iodine isotopes are rapidly absorbed from the gastrointestinal tract. Their toxicity depends on their accumulation in the thyroid gland. In view of the thyroid gland's small mass, iodine's specific radioactivity in the thyroid gland is hundreds and even thousands of times above its level of activity in other organs.

A great deal of experience has been accrued in the area of using different agents to prevent the accumulation of radioactive iodine in the thyroid gland in humans. Most researchers agree that potassium iodine in the

form of 100-mg tablets is a most suitable agent for preventing the accumulation of radioactive iodine in the body. When ^{131}I and potassium iodide are administered simultaneously, less than 3 percent of the administered dose of the isotope is accumulated in the thyroid gland. In addition to potassium iodide, potassium perchlorate is also effective. Nevertheless, these preparations are much less effective if administered after ^{131}I has already entered the body. In view of that fact, combined methods for removing ^{131}I have been proposed that include the administration of sodium iodide and sodium perchlorate in conjunction with osmotic diuresis.[4] To date, however, many questions regarding accelerating excretion of radioactive iodine from the body still remain unanswered.

Long-lived ^{89}Sr and ^{90}Sr are the most toxic of the strontium radionuclides formed during nuclear explosions. The reason that entry of radioactive strontium into the body poses so great a threat is because of the ease with which it is absorbed from the lungs and gastrointestinal tract. Resorption of strontium in the gastrointestinal tract is completed within 5 hours, and resorption from the lungs is completed in 6 hours.[5] Once strontium has been absorbed into the blood and lymph, it is selectively accumulated in the skeleton. As much as 62 percent of the amount that enters the body accumulates in the bones.

Removing radioactive strontium from the body is a difficult problem. Despite the very large number of studies devoted to the problem, no effective methods have been found to date. Among agents accelerating excretion of strontium, salts of stable strontium and complex-forming agents merit attention. They act in accordance with the principle of isotope dilution. However, toxic doses of stable strontium must be administered to obtain a clear effect. The most effective complex-forming agents for removing radioactive strontium are diaminodiethyl ether tetraacetic acid and diaminodiethylsulfide tetraacetic acid. There are data indicating that cellulose-immobilized DTPA possesses enhanced strontium-binding activity.[6]

In view of the lack of any highly effective preparations, the use of combinations of several agents is interesting. There are indications in favor of using parathyrecrine with EDTA, diaminodiethyl ether tetraacetic acid, and diaminodiethylsulfide tetraacetic acid and using sodium citrate with the simultaneous administration of calcium gluconate. Calcium is capable of increasing the excretion of strontium both in the early period and 2 weeks after the administration of strontium. The combined administration of calcium and ammonium chloride 2 weeks after administration of the isotope causes a three- to fourfold increase in strontium over the control level. Yugoslav researchers[7] have demonstrated that integrated therapy involving the use of calcium alginate, ferrocyanine, potassium iodide, and Zn-DTPA reduced absorption of radioactive strontium; however, those results were not confirmed by Hodgkinson,[8] who believes that such treatment may be effective only in the case of integral contamination by several radionuclides.

At the present time, the use of adsorbing binding agents, including edible fibers (bran and pectins), is a more effective method of removing radioactive strontium from the body. Pectins are weakly acidic ion exchangers. The carboxyl groups of the galacturonic acids that are components of polysaccharide are capable of attaching polyvalent cations, thereby forming metal pectins. The results that have been obtained with regard to the binding of strontium with pectins in the gastrointestinal tract are contradictory. According to A.A. Rubanovskaya's data,[9] sunflower pectin reduced skeletal levels of ^{90}Sr by 31-48 percent in young rats and by 17-30 percent in adult rats. According to data gathered by N.O. Razumovskiy,[10] sunflower and beet pectins demonstrated an identical result, decreasing the Sr content in rats' bodies by 20-45 percent. When administration of pectins was delayed 1 hour, their effectiveness decreased by 10-20 percent. In experiments with stable strontium chloride, pectins were not very effective.[11] No decrease in accumulation of radionuclides was observed upon simultaneous administration of a model mixture of fission products and a standard sample of pectin.[12]

A pectin-vitamin powder that included a natural mixture of pectin, cellulose, and P, B, PP, and C group vitamins turned out to be effective.[13] In experiments on female nonpedigree white rats, administration of 350 mg of the pectin-vitamin powder in the rats' daily food allowance reduced the accumulation of ^{90} in their bodies on day 30 of the experiment by 56.6 percent as compared with the level of accumulation in the controls.

L.N. Ovsyannikov[14] demonstrated that when animals are given apple, beet, and citrus pectin, binding of radioactive strontium in their bodies is increased by a factor of 2-3 as compared with the level of binding in controls. Methoxylated pectins (calcium pectin) have been proposed for binding strontium in humans. Alginates, i.e., salts of alginic acid that are found in brown algae, bind strontium effectively, as has been demonstrated by numerous studies conducted in different countries.[15,16,17,18]

Alginic acid is present in algae in the form of a high-molecular weight polysaccharide consisting of monomers of D-mannuronic and L-guluronic acids (as published). It has been hypothesized that the affinity of alginate and strontium is dictated by the guluronic component. It has been demonstrated that alginate is

capable of significantly reducing biological absorption of strontium entering the animal and human bodies via the inhalation or oral routes.[19,20,21]

A process for obtaining guluronic acid-enriched modified calcium alginate that binds radioactive strontium at a level of 90 percent has been developed at the Biotechnology Scientific Production Association.[22] According to the authors, the preparation's high level of activity may be explained by the fact that both ion exchange and complexing with *Sr* are characteristic of alginates.

Studies of the possibility of using sodium and calcium alginate-enriched foodstuffs to reduce the accumulation of ^{90}Sr have been conducted at the Ukrainian Center for Research on Radiation Medicine.[23] It has been demonstrated in experiments on female nonpedigree white rats that sodium alginate reduced the strontium accumulation factor from 9.74 in controls to 2.59 (26.6 percent) when administered in the daily food allowance at a dose of 0.4 g/animal and to 4.22 (43.3 percent) when added in a dose of 0.2 g/animal. Calcium alginate turned out to be more effective: The radionuclide accumulation factor was reduced to 1.29 (12.9 percent). Adding apple powder (3 percent) and pectin (5 percent) to the diet together with sodium alginate intensified the latter's effect: the ^{90}Sr accumulation factor amounted to 2.24 (23 percent).

Foods made of alginate-containing brown algae also reduced the accumulation of radioactive strontium.[24] In experiments on white rats, preserves and jam made from the algae *Laminaria japonica* reduced absorption of strontium by a factor of 1.8-4.3. Adding dried algae to animals' daily food allowance also reduced the dose of internal irradiation of their bodies. The authors believe that using products of the said algae in food may also reduce the accumulation of radioactive strontium in the human body.

Experimental studies involving the use of foodstuffs made from laminaria were also conducted in the Laboratory for Prophylaxis of Internal Irradiation at the All-Union Radiation Medicine Research Center of the USSR Academy of Medical Sciences.[25] Appetizer preserves with onion, vegetable oil, and acetic acid added to the laminaria were tested along with jams made from laminaria and a dried laminaria made from algae that was finely chopped and held in a brine solution with spices. The tests were conducted in a radiation vivarium on nonpedigree female white rats weighing 140-160 g. Their diet was balanced from the standpoint of calories derived from protein, fat, and carbohydrates and included oats, vegetables, cereal, cottage cheese, meat, and bread.

Animal studies have shown that when foodstuffs made from laminaria are used, the same effect is observed as when calcium alginate and alginic acid are used. Including laminaria preserves in animals' daily food allowance 5 hours after the isotope had entered their bodies still produced an effect; however, it was weaker. The alginic acid of laminaria and its salts blocked the uptake of radioactive strontium to a lesser degree than when the food product and radionuclides were administered simultaneously.

A formula and process for producing nonalcoholic beverages possessing a radioprotector effect and helping the body resist infections and intoxication have been developed. The beverages include vitamins, trace elements, and radionuclide-binding polymers of natural origin.[26] It has been proposed that these beverages be used for therapeutic and prophylactic purposes for organized population groups: at pediatric institutions, enterprises with toxic work environments, nuclear power plants, and so forth.

Highly oxidized celluloses made from wastes generated by the cotton-spinning and weaving industries have also proved effective.[26] Experiments on rats have demonstrated that the highly oxidized celluloses form stable complexes with radioactive strontium that are not broken down in the gastrointestinal tract and that do not diffuse through the intestinal walls, thanks to which radionuclide deposition in the skeleton is reduced.

The ability to bind radioactive strontium increases as the number of carboxyl groups increases. The authors demonstrated that the protective effect of highly oxidized cellulose when used prophylactically significantly surpasses the effectiveness of pectin and sodium alginate. Another derivative of the polysaccharide chitin, namely, chitosan, has been noted to accelerate the elimination of radioactive strontium.[27]

^{137}Cs is the most significant of the cesium radionuclides formed upon the fission of uranium and plutonium. After strontium, cesium is the most dangerous isotope to humans. It may accumulate in certain plants and ultimately enter foodstuffs. Its danger lies in its high level of resorption in the gastrointestinal tract and lungs.

Various preparations are used to eliminate radioactive cesium. One may create "relationships of competition" with cesium in the body or induce isotope dilution. Among such preparations are salts of stable cesium, potassium, and sodium. Furthermore, the use of a series of other therapeutic agents to accelerate excretion of the nuclide has been attempted even though substantiating the feasibility of their use on the basis of the mechanisms of their effect is rather difficult. Among the said agents are parathyrectine, vitamin D_3, and unestrol.

Experimental studies that have been conducted both in our country and abroad have made it possible to recommend the ion exchanger iron ferrocyanide (ferrocin, cesium radiogardase, Berlin blue, Prussian blue) as the most effective agent for removing cesium.[28,29] The ability of food products containing ferrocin (20 mg/animal) to reduce ^{137}Cs levels to 7-8.3 percent has been demonstrated in experiments on male white rats. When included in food products, ferrocin reduces ^{137}Cs uptake by 90-93 percent.

On the basis of those experiments, ferrocin's "disincorporating" activity when used in drug or food additive form was tested in 16 people. The degree of elimination of ^{137}Cs from the body ranged from 1.75 percent to 2.89 percent as compared with 0.5 percent in the controls. The authors recommended using ferrocin-containing foodstuffs in population centers with a high level of radionuclides.[30] Positive results have also been achieved with other hexacyanoferates[29,31]; however some of them have turned out to be carcinogenic. Pectin,[32] alginate,[33] and carbulose[34] may be used as sorbents for binding radioactive cesium. When radionuclide contamination of the environment after the Chernobyl accident was measured, levels of other radionuclides besides strontium and cesium were also recorded, for example, radioactive barium, lanthanum, zirconium, ruthenium, and several elements with a high Z number.[35] Elimination of these radionuclides is also very important.

The effectiveness of chelating agents (DTPA, quinolinamide, and so forth) has been noted in animal experiments involving ^{239}Pu and ^{241}Am. The greatest effect was achieved when methyleneiminodiacetocatechol was administered.[36] A comparative study of the effectiveness of the salts CaDTPA and ZrDTPA in eliminating thorium nitrate from the bodies of 3-month-old rats demonstrated that all other conditions being equal, CaDTPA manifested a higher level of activity.[37]

Administration of ZnDTPA turned out to be effective in preventing the development of long-range radionuclide effects induced when ^{241}Am was administered to mice of the line C57B1. Extended treatment with this chelating agent reduced the incidence of bone tumors and liver cancer and the total number of malignant tumors by reducing the concentration of ^{241}Am. Administration of DTPA also extended the lives of the mice.[38]

When administered in doses of 30 μmol/kg, the chelating agents DFO-HOPO (a hydroxypyridine derivative of deferoxamine) and DTRA-DX [as published] (a dihydroxamine derivative of DTPA) reduced the levels of ^{239}Pu and ^{241}Am in the organs and tissues of 3-month-old female rats by up to 8 percent as compared with the levels in untreated controls.[39] An attempt to eliminate ^{241}Am from humans by intravenous infusion of DTPA also produced positive results. The amount of isotope excreted with the urine and feces was increased by a factor of 4-11.[40]

In experiments involving ^{239}Pu, complex compounds of hydroxypyridononate, deferoxamine, and polycatechoylate were simultaneously administered to mice. Removal of the nuclide amounted to more than 70 percent. Twenty-four hours after ligands had been administered, the effectiveness of removal of the nuclide amounted to only 5 percent.[4] Ethane-1-hydroxy-1,1-diphosphonate has also been demonstrated to have a protective effect on bone formation under conditions of exposure to uranyl nitrate. The preparation's stimulating effect is due to the fact that it blocks entry of the nuclide into the bone's healing zone.[42]

When used in combination with DTPA, tiron [transliteration] (sodium 4,5-dihydrobenzidine-1,3-disulfonate) reduced the level of uranyl nitrate in the organs and tissues of 4-month-old female rats when they were exposed to a level of uranyl nitrate 12 times greater than the maximum permissible concentration for humans. Tiron became more effective as its dose was increased, with the peak effect occurring upon administration of 1,000 μmol/kg. The authors believe that it is possible to use tiron in cases where workers are suffering from acute uranium poisoning.[43]

Food additives and biologically active materials constitute a unique group among preparations intended to eliminate radionuclides. The mechanism of their effect still remains unclear. V.A. Knizhnikov has studied the effect that adding fish paste to animals' daily food allowance has on accumulation of ^{90}Sr in the skeleton. The use of fish paste reduced the accumulation of radioactive strontium by 70 percent as compared with the levels of accumulation in controls. The paste Okean [ocean] also facilitated elimination of radioactive strontium but had no effect on elimination of cesium.[44]

Studies of the use of natural zeolites to accelerate excretion of radioactive strontium and reduce its accumulation in bones also merit attention.[45] A salad made of the seaweed known as tangle, a jam made from laminaria, and marine mussel hydrolysate have all produced positive effects when used as therapeutic and prophylactic agents in cases where humans have been subjected to internal irradiation.[47]

Interesting results have been obtained by using redbud extract (a member of the legume family) as a radionuclide-removing agent.[48] It has been hypothesized the preparation's effectiveness is dictated by the chemical affinity of the components of redbud with radioactive

materials. Active extracts have been obtained from all parts of the plant.

In conclusion, it should be noted that despite the definite progress that has been made in the area of eliminating radionuclides from the body, many problems remain unresolved. Above all, the possibilities of removing radionuclides from the respiratory tract have not yet been studied sufficiently. No adequately effective preparations for accelerating the excretion of radioactive strontium have yet been found. Agents reducing the absorption of such products of the fission of uranium as tellurium, molybdenum, and ruthenium by the gastrointestinal tract must be found.

References

1. H.S. Martiland, R.E. Humphries, ARCH. PATHOL., Vol 7, 1929, p 406.

2. J. Schubert, SCIENCE, Vol 105, p 389.

3. C.A. Adams, J.A. Bonell, HEALTH PHYS., Vol 7, 1962, p 127.

4. Yu.F. Koval, Uskoreniye vyvedeniya iz organizma radioaktivnykh isotopov (Accelerating Excretion of Radioactive Isotopes From the Body), Moscow, 1972.

5. D.I. Semenov, N.D. Borisova, TRUDY INSTITUTA BIOLOGII URALSKOGO FILIALA AN SSSR, No 12, 1960, p 25.

6. R.A. Bulman, O. Vanderborght, and Van Puymbrick, HEALTH PHYS, Vol 44, 1983, pp 422-430.

7. Krista Kostial, Biserka Kargacin, Jvon Simonovic, HEALTH PHYS., Vol 52, 1987, pp 371-372.

8. A. Hodgkinson, B.E.C. Nordin, J. Hambletom, CAN. MED. ASSOC. J., 1967.

9. A.A. Rubanovskaya, GIG. TRUDA I PROFZAB., No 4, 1961, pp 43-47.

10. N.O. Razumovskiy et al., Sbornik referatov po radiatsionnoy meditsine (Collection of Abstracts on Radiation Medicine), Moscow, 1959, C7100.

11. D. Waldron, T. Paul, S. Scoryne, NATURE, Vol 205, No 4796, 1965, pp 1117-1118.

12. O.D. Livshits, GIG. I SANIT., No 3, 1986, pp 85-86.

13. A.Ye. Romanenko, I.B. Derevyago, et al., GIG. TRUDA I PROFZAB., No 12, 1991, pp 8-10.

14. L.N. Ovsyannikov, et al., Itogi otsenki meditsinskikh posledstviy avarii na Chernobylskoy AES (Results of an Assessment of the Medical Consequences of the Accident at the Chernobyl Nuclear Power Plant), Kiev, 1991, pp 164-165.

15. O. Vanderborght, S. Van Puymbroeck, HEALTH PHYS., Vol 35, No 8, 1978, pp 255-258.

16. A. Van Barneveld, S. Van Puymbroeck, O. Vanderborght, HEALTH PHYS., Vol 33, 1977, pp 533-537.

17. D. Waldron-Edward, CAN. MED. ASSOC. J., Vol 99, 1968, pp 986-992.

18. Y. Tanaka, D. Waldron-Edward, et al., CAN. MED. ASSOC. J., Vol 99, 1968, pp 169-175.

19. A. Sutton, NATURE, Vol 216, 1967, pp 1005-1007.

20. J.M. Light, G.K. Stokey, et al., CAN. MED. ASSOC. J., Vol 95, 1966, pp 532-534.

21. [No reference no. 21 included in reference list.]

22. G.K. Korotayev, et al., Tezisy dokl. 4-oy Vsesoyuzn. konf. "Khimiya, farmakologiya i mekhanizm deystviya protivoluchevykh sredstv" (Abstracts of Fourth All-Union Conference Titled "Chemistry, Pharmacology and Mechanism of the Effect of Anturadiation Agents"), Moscow, 1990, pp 96-97.

23. V.NYe. Korzun, Yu.G. Voronova, et al., MED. RADIOL., No 5-6, 1992, pp 31-34.

24. Yu.G. Voronova, N.I. Rekhina, et al., RYBNOYE KHOZYAYSTVO, No 7, 1991, pp 65-66.

25. V.G. Ivanisenko, et al., Realizatsiya nauchnykh dostizheniy v praktike farmatsii: Tez. dokl. resp. nauch. konf. (Implementing Scientific Progress in Pharmaceutical Practice: Abstracts of Reports Presented at the Republic Scientific Conference), 16-18 October 1991, Kharkov, 1991, pp 79-80.

26. Z.S. Nasyrova, et al., Materialy res. nauch.-tekhn. konf. "Okhrana i ratsionalnoye ispolzovaniye vodnykh resursov atmosfernogo basseyna i otkhodov proizvodstva" (Protection and Rational Use of the Water Resources of the Atmospheric Basin and Industrial Wastes), Kyrgyzstan SSR State Committee for Environmental Protection, Frunze, 1991, pp 162-163.

27. Nishimura Yoshikazu, Wiu In Sun, et al., RADIOISOTOPES, Vol 40, No 6, 1991, pp 244-247.

28. P.P. Nielsen, R. Fisher, et al., EXPERIENTIA, Vol 44, 1988, pp 502-504.

29. Borisov, et al., GIG. I SANIT., No 4, 1989, pp 19-21.

30. V.N. Korzun, MED.-RADIOL., No 5, 1991, pp 23-27.

31. P. Nielsen, Bernd Dresow, et al., NUCL. MED AND BIOL., Vol 18, No 7, 1991, p 821-826.

32. G.A. Altukhova, et al., Metabolizm i biologicheskoye deystviye radionuklidov pri oralnom postuplenii v organizm (Metabolism and Biological Effect of Radionuclides Upon Entry Into the Body via the Oral Route), Moscow, 1989.

33. K. Kostial, B. Kargacin, et al., THE SCIENCE OF THE TOTAL ENVIRONMENT, Vol 12, 1981, p 1.

34. A.F. Tishchenko, et al, Itogi otsenki meditsinskikh posledstviy avarii na Chernobylskoy AES (Results of an Assessment of the Medical Consequences of the Accident at the Chernobyl Nuclear Power Plant), Kiev, 1991, pp 217-218.

35. Radionuclides Found in Sweden, private communication, 1986.

36. M.C. Luo, V. Volf, INT. J. RAD. BIOL., Vol 55, No 4, 1988, pp 679-688.

37. G.N. Stradling, J.C. Moody, et al., INT. J. RADIAT. BIOL., Vol 59, No 5, 1991, pp 1269-1277.

38. [No reference no. 38 included in reference list.]

39. [No reference no. 39 included in reference list.]

40. H.D. Roedler, D. Nobker, et al., RADIAT. PROT. DOSIM., Vol 26, No 1-4, 1989, pp 377-378.

41. P.W. Durbin, N. Yeung, et al., RADIAT. PROT. DOSIM., Vol 26, No 1-4, 1989, pp 351-358.

42. M. Ubios Angela, et al., ARCH. ENVIRON. HEALTH, Vol 45, No 6, 1990, pp 374-377.

43. G.N. Stradling, S.A. Gray, et al., HUM. AND EXPER. TOXICOL., Vol 40, No 3, 1991, pp 195-198.

44. V.A. Knizhnikov, VOPR. PITANIYA, No 2, 1991, p 40.

45. V.G. Bardov, et al., Itogi otsenki meditsinskikh posledstviy avarii na Chernobylskoy AES (Results of an Assessment of the Medical Consequences of the Accident at the Chernobyl Nuclear Power Plant), Kiev, 1991, p 18.

46. P. Mizik, M. Mokosova, RADIOACTOV A VIVOT POSTRED., Vol 3, 1990, pp 121-127.

47. V.N. Korzun, Nauchno-prakticheskiye aspekty sokhraneniya zdorovya lyudey, podvergshikhsya radiatsionnomu vozdeystviyu v rezultate avarii na ChAES (Scientific-Practical Aspects of Maintaining the Health of People Subjected to Radiation as a Result of the Accident at the Chernobyl Nuclear Power Plant), Republic Conferences, 12-14 Minsk 1991, Minsk, 1991, pp 18-19

48. Patent Application 3 741994, Germany, ICP A 61 K 35/37, A 61 K 33/34

Russia: Case of Extremely Severe Intestinal Form of Most Acute Radiation Sickness

964D0739A Moscow MEDITSINSKAYA RADIOLOGIYA I RADIATSIONNAYA BEZOPASNOST in Russian Vol 40 No 4, Jul-Aug 95 pp 6-11

[Article by G.I. Alekseyev and V.I. Rukhlyadev; Military Medical Academy, St. Petersburg; manuscript received 5 Jul 93]

[FBIS Summary] The case of an extremely severe form of highly acute radiation sickness has been reported. The patient, a 54-year-old male operator of a gamma-unit, was involved in an accident resulting from flagrantly violating the safety regulations specified for operating an industrial cobalt source with a total activity of 600,000 Ci. It was determined that he had been gamma-irradiated for 20-30 seconds in a dose of 15 to 20 Gy. The patient died on day 10 after having been irradiated. Before his death, he received a variety of treatments, including bone marrow transplantation, hemoperfusion, and anti-infectious and antihemorrhagic drug therapy. The treatments and the patient's response to each of them on each of the days preceding his death were detailed. It was determined that gastrointestinal and asthenohypodynamic syndromes developed in the patient immediately after he had been exposed to the gamma-irradiation. Within a few hours after the accident, the patient exhibited such indicators of extremely severe radiation sickness as fever, skin rash, subictericity of the sclerae, and conjunctival injection. Soon after the accident, pronounced and increasing symptoms of toxic-hypoxic encephalopathy and general toxemia developed, as did significant impairment of hematopoiesis. An autopsy revealed that he had suffered an intestinal form of acute radiation sickness, bone marrow devastation, necrosis of his esophageal and intestinal epithelium, and spermatogenesis depression. The autopsy also established that the transplanted bone marrow had begun implanting in the patient's body. The signs of the said implantation were most distinct in the patient's spleen, lymph nodes, and tonsils. The patient was said to be the first radiation victim to be treated with hemosorption. Hemoperfusion was performed on day 1 at a blood flow rate of 50-75 ml/min. A total of 19 liters and 400 ml of blood was perfused. Even while the hemosorption procedure was still in progress, the patient began to feel better and his body temperature decreased from 37.1°C to 36.6°C. Although it did not save the patient's life, the hemosorption procedure had a clearly positive effect on the clinical and laboratory indicators of his general toxemia. Tables 2; references 4: 3 Russian, 1 Western

Russia: Methods of Labeling Monoclonal Antibodies With Various Radionuclides

964D0739B Moscow MEDITSINSKAYA RADIOLOGIYA I RADIATSIONNAYA BEZOPASNOST in Russian Vol 40 No 4, Jul-Aug 95 pp 67-72

[Article by V.A. Zerzhanina, L.N. Korsakova, O.Yu. Mirolyubova, and N.P. Fadeyev, Central X-ray-Radiologic Scientific Research Institute; manuscript received 27 May 93]

[FBIS Summary] Existing methods of labeling monoclonal antibodies [MoAbs] with radionuclides may be classified as either direct or "indirect" methods. Among the main criteria for selecting the labeling method in each specific case are the following: retention of the protein's immunologic activity after labeling; susceptibility of the molecule to oxidation; satisfactory specific activity; kinetics of the labeling process and bond between the MoAb and radionuclides (it should remain stable under in vivo conditions); purpose of the labeling (diagnostic, pharmacokinetic, scientific prediction); physical characteristics of the radionuclide (half-life, particle energy, specific activity); chemical reactions required to incorporate the radionuclide into the MoAb molecule; and dose of radiation incurred by the patient's (animal's, researcher's) organs. Iodine isotopes (^{125}I, ^{131}I, and ^{123}I) are the most widely used isotopes for labeling MoAbs. The main methods of labeling MoAbs with iodine isotopes are isotope exchange and electrophilic substitution. A third method entails attaching the iodine at the double bond of the protein molecule; however, it is used rarely because the resultant labeled compound is often unstable in vivo. Of the various methods described, electrophilic substitution with chemical, enzyme, or electrochemical oxidation is best. Attempts to label the MoAbs MA-5, MA-10, and MA-20 (which are active against insulin receptors) have been most successfull when iodogen has been used as the oxidizing agent. One big drawback of labeling MoAbs with radioactive iodine is the resultant dehalogenation of the labeled MoAbs, which in turn results in the accumulation of high levels of radioactivity in the thyroid gland and other organs. New methods of labeling MoAbs with iodine are being developed that result in the release of smaller amounts of free iodine. According to one proposed method, the radioactive iodine-labeled MoAbs are subjected to gel filtration with different grades of Sephadex and column chromatography. "Direct" methods of labeling MoAbs with ^{77}Br, ^{211}At, and ^{188}Re have also been described. In addition, reports of "indirect" radiolabeling of MoAbs by using bifunctional chelates have begun appearing during the past decade. Specifically, there have been reports of labeling MoAbs with such metals as ^{67}Ca, ^{111}In, ^{99m}Tc, ^{90}Y, ^{57}Co, and ^{59}Fe. The molecules of the bivalent chelates form rather stable covalent bonds with proteins. Ethylenediamine tetraacetic acid [EDTA], diethyleneamine triaminepentaacetic acid [DTPA], and their many derivatives are most often used as chelates, and the chelation reaction is generally conducted in Tris-buffer (pH 8.5). The labeling procedure is a relatively simple two-stage procedure involving (1) modification of the chelate (to obtain anhydrides, amides, etc.) and (2) reaction of the modified chelate with the MoAb to form a covalent bond, after which the resultant product is purified by column chromatography or some other method. The chelate is conjugated with a specific region of the MoAb in such a way that the resultant MoAb-conjugate retains its antigen-binding ability. ^{111}In and ^{99m}Tc are the radionuclides that have been most studied for use with the indirect labeling technique. A third method of labeling MoAbs has also been reported, namely, a metabolic method that involves growing hybridomas in the presence of ^{14}C-, ^{3}H-, or ^{35}S-labeled amino acids. The resultant labeled MoAbs completely retain the properties of the initial protein. The problem of obtaining new radioisotope-labeled MoAbs thus continues be the subject of intensive research. Figure 1, table 1; references 77: 5 Russian, 72 Western.

Russia: Using a Pentapeptide (YFRKD) To Inhibit the Complex Conditioned Reflex Activity in the Ontogenesis of White Rats

964D0736A St. Petersburg FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I.M. SECHENOVA in Russian Aug 95 Vol 81 No 8, pp 147-151

[Article by N.A. Ryabchikova and G.I. Chipens, Higher Nervous Activity Chair, Biology Department, Moscow State University, Moscow; manuscript received 15 Feb 95, UDC 612.599.323.4+612.821.6+612.8.015]

[FBIS Summary] It is believed that immunohormones, like interferons, are precursors of peptides that function as intermediaries in immunoneuroendocrine reactions. The model pentapeptide Tyr-Phe-Arg-Lys-Asp [YFRKD] is formed by combining the highly polar C-terminal tripeptide of interferon-α [RKD] with the hydrophobic apolar dipeptide [YF], which preferentially becomes part of the interferon's active center, as a result of which it reacts with cell membranes. Interferon is known to possess psychotropic properties, and it has been hypothesized that interferon interferes with the acquisition of new information if it is administered to animals during the learning process. That hypothesis was tested in an experiment performed on 23 nonpedigree white rats aged 15 to 17 days at the start of the experiment and 1.5 months at the end of the experiment. First, all the rats were conditioned to perform the first step of a two-step routine for obtaining food. The rats were then divided into experimental and control groups

(of 13 and 10 rats, respectively). The rats in the experimental group were given intramuscular injections of YFRKD (16 μg per rat or 80 μg/kg body weight in a 0.4 ml solution) 30 minutes before each subsequent training session. During those subsequent training sessions, the rats were taught a second set of actions that they were to "wedge" into the food procurement process that they had previously been taught. Thirty minutes before they too were taught the second set of actions, the controls received a physiologic solution in the same volume as the YFRKD had administered to the experimental rats. The experiments established that when YFRKD is administered to rats before they receive training, it affects both their incorporation of past experience into newly learned behavior and their ability to learn new material. The YFRKD had a greater effect on the rats' ability to execute the procedure that they had previously been taught than it did on their ability to learn new behaviors. Although rats that had received the YFRKD had more difficulty performing the previously learned portion of the food procurement routine after learning the second portion than did the control animals, both groups of animals manifested similar degrees of retention of the conditioned reflex after a 2-week break in the experiment. It was concluded that the experiment did not confirm the initial hypothesis that interferon-α affects the process of acquisition of new information but that it did confirm that the simple peptide formed from hydrophobic (YF) and polar (RKD) amino acids modulates the complex processes of reinforcement and inhibition of conditioned reflex responses. Figures 3; references 5: 2 Russian, 3 Western.

Russia: Neuropeptides: Mechanisms of Their Effect on the Brain's Integrative Activity

964D0736B St. Petersburg FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I.M. SECHENOVA in Russian Aug 95 Vol 81 No 8, pp 158-161

[Article by L.A. Severyanova, I.I. Bobyntsev, Yu.D. Lyashev, and D.V. Plotnikov, Pathologic Physiology Department, State Medical University, Kursk; manuscript received 1 Feb 95; UDC 612.82/.83+557.15/.17]

[FBIS Summary] The mechanism of the effect of neuropeptides on the brain's integrative activity was examined in a study of the effects of 20 analogues of hypothalamohypophysial peptides (gonadotropin-releasing factor, the n-terminal fragment of adrenocorticotropic hormone [ACTH], enkephalins) and tuftsin on pain sensitivity, learning, memory, motivation, and emotion. During the individual experiments, rats were subjected to various types of training. They were trained in a T-shaped labyrinth with food serving as a reinforcement, and they were trained to actively avoid pain in a three-chamber device in which they received painful electric shocks. In the different experiments, the rats were injected with the various peptides intraperitoneally or intragastrically 10 to 20 minutes before the training. Six mechanisms of behavioral peptidergic effects were established during the various experiments. First, it was established that peptides' effects on aggressive-defensive behavior depend on the presence of key amino acid radicals in the peptide molecule. Specifically, peptides containing an arginine radical intensify aggression and generally possess an algesic effect. Second, peptides possessing an algesic, anxiogenic, and aggressogenic effect were found to primarily increase the excitability of the brain's negative emotion system. Specifically, pronounced aggression was observed both when pain sensitivity was increased (by arginine-containing analogues of ACTH, gonadotropin-releasing factor, and leu-enkephalin) and when it was reduced (by analogues of enkephalin and tuftsin). Decreased aggression was also observed in the absence of an analgesic effect (by leu-enkephalin analogues not containing arginine), thus indicating that behavior induced by pain stress depends on excitability of the brain's negative emotion system more than it depends on pain reception. Third, it was demonstrated that the behavioral effect of one and the same peptide may depend on its predominant effect on specified brain structures; for example, the statistically significant increase in aggressive-defensive behavior observed after intraperitoneal injection of the superactive analogue of gonadotropin-releasing factor (surfagon in doses of 0.15 and 50 μg/kg body weight) may be due to the fact that it mainly affects the hypothalamus, whereas the opposite effect when surfagon is injected into the brain's lateral ventricles may be due to the fact that it mainly effects the limbic structures and central gray matter of the mid-brain. Fourth, neuropharmacologic analysis confirmed that the mechanism of the effect of analogues of ACTH and opioid peptides on behavior during pain stress includes modulation of the activity of the brain's muscarinic system. Fifth, during learning, neuropeptides exerted a differentiated effect on the motivation systems and mechanisms responsible for the brain's closure function and consolidation. For example, leu-enkephalin in a dose of 1 μg/kg body weight improved learning, whereas larger doses of the same compound or a more active analogue had an adverse effect on the rats' food procurement and pain avoidance. Sixth, the peptidergic effects of the analogues studied depended on the animals' typological features. For example, the effects of the neuropeptides studied were significantly more pronounced in the short-sleeping rats than in the long-sleeping rats. Table 1; references 6: 4 Russian, 2 Western.

Paid Health Services in the Public Health System of Kazakhstan

964D0774A Almaty ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian Aug 95 No 8, pp 4-8

[Article by M. K. Kulzhanov, M. A. Mumunov and A. V. Novikov, Republic of Kazakhstan Ministry of

Health, South Kazakhstan Oblast Administration Health Department; UDC 614.2(574)]

[FBIS Translated Text] There are now serious problems in funding institutions of Kazakhstan's health service, and in providing them with medications, food, medical equipment and ambulances, resulting in a decrease in the volume, level and quality of health care. State budget allocations were cut dramatically. At this moment the republic's public health system is able to support only a minimum volume of health care, owing to which the health indicators of the population are worsening.

This situation is also typical of South Kazakhstan Oblast.

The law "On Protecting the Health of People in the Republic of Kazakhstan" (1992) foresees a diverse economic structure for public health permitting introduction of diverse forms of care, including paid health services. The principle by which the public health budget is formed and financed must be changed as a consequence, with regard for market interrelationships. At the same time the RK [Republic of Kazakhstan] Constitution ignores this unavoidable phenomenon of the marketplace, making no stipulations regarding it.

To obtain supplementary financing sources, the Kazakhstan Ministry of Health started an experiment jointly with the Health Department of the South Kazakhstan Oblast Administration, in which some public health services were made self-supporting. The results of a large number of programs conducted in the oblast up to 1993 were positive. Developing this activity, we foresaw introducing mandatory health insurance to the oblast starting in 1994, also as an experiment.

We concurrently determined the main aspects of reforming public health: raising accessibility, expanding volume and improving the quality of health care to the population while, improving the work of medical personnel.

A system was planned for implementing the reforms that would guarantee an increase in the volume of resources to support the needs of public health, ensure effective use of these resources, and protect the interests of broad segments of the public. This strategy was made possible by successful implementation of the mandatory health care program introduced in the oblast, of which paid health services is a harmonious part.

In selecting the public health institutions to be transferred to paid services, we based ourselves on the idea that a certain fraction of health care must remain free of charge, so as to avoid any decrease in the demand for services because of their inaccessibility. Joint introduction of the system of paid medical services and mandatory health insurance was defined as the optimum variant. As a consequence the system of combined payments called for in the experiment presupposes integrated payments for services rendered and for insurance policies of the mandatory health insurance system, but the bulk of the payments must be charged to mandatory health insurance, which is especially important to the socially unprotected segments of the population.

In order to see how realistic the project is, the directors of six Shymkent medical institutions were surveyed jointly with the leadership of the "Health Reform" program (1995): the observation polyclinic of a dermatological and venereological dispensary, a diagnostic center, an emergency hospital, an eye hospital, the Avtomobilist cost-accounting medical unit, and a cost-accounting dental polyclinic. Executives of the health department and city authorities responsible for the work of medical institutions were also surveyed. The grounds and viability of the "Program to Introduce the Principles of Self-Financing" was the subject of the survey. Four of the noted institutions—the dermatological and venereological dispensary's observation polyclinic, the diagnostic center, the eye hospital and the emergency hospital—had a combined financing source (fees for health services rendered, plus budget appropriations). The main and only financing source of the two other Shymkent medical institutions—the Avtomobilist cost-accounting medical unit and the cost-accounting dental polyclinic—was fees for services rendered and, in part, receipts from third parties.

We foresaw conclusion of agreements with the enterprises, acquisition of resources under mandatory health insurance, and direct payments by the users of the health services themselves, which provided monetary resources additional to those from the state budget.

The income of the medical institutions with a combined financing source is of special interest. In our experiment the share of income received as a result of implementing the self-support principle in medical institutions with combined financing sources was from 1 to 8 percent, which was a small fraction of the overall budget (8-64 million tenge). However, resources obtained in this fashion were placed completely at the disposal of the director of the medical institution, and were used at his discretion, with no outside control over expenses pertaining to budgeted items, which is especially valuable to the institution.

Significant difficulties arose in determining the methods for setting the rates for paid services. The rates for particular medical services were set in all medical institutions with regard for anticipated expenses on primary resources, including wages, income tax, contributions to the public social safety net fund, medications, municipal needs, outlays on use of premises, and overhead. Periodic adjustments were made to account for inflation. Although we have not completed our study of the

mechanism for setting the rates, we feel that its basic methods are justified.

Profit received from implementing the principle of self-support in medical institutions with a combined financing source was used by us to raise the wages of the associates of these institutions, to acquire additional drugs and equipment, and to improve production conditions.

With the help of the leadership of the "Health Reform" program we were able to compare our results of using a system of paid health services with world experience.

World Experience	South Kazakhstan Oblast:
1. People in different socioeconomic segments of the society are now spending sizable amounts of money on public health (acquisition of medicines and medicinal herbs and resources from private vendors, unaccounted fees for granted services). Such expenses are often accompanied by far from the most effective return.	1. Experience shows that there are cases in the oblast in which a user of services resorts to folk medicine or pays for the services of private medical workers in order to reduce waiting time or receive better health care. A more complete picture of consumer outlays should become available after the results are in on an analysis of the structure of the family budget being conducted by the health department.
2. Money received in payment from consumers may supplement existing financing sources (for example budget appropriations or insurance payments).	2. It was found in 1993 in the course of self-financing of some of the oblast's medical institutions that the aggregate income of four institutions functioning on the basis of the principles of joint financing was from 1 to 8 percent of the total amount of budget appropriations. Nonetheless, this relatively small profit was of considerable interest to the directors of medical institutions because the money earned in this fashion could be used to purchase basic necessities, and to provide material incentives to personnel.
3. Consumers and institutions can use the level of payment for health services as an indicator of the cost of the rendered services, and as an indicator of the demand for them. Moreover the rates for some services may be made artificially low compared to the costs so as to promote preventive services and provide health care to persons with chronic and infectious diseases.	3. The oblast's medical institutions established rates on services in proportion to the cost of expended resources. As a consequence consumers, or the entities that made the payments for them (usually enterprises), were able to get a sense of the cost of services. Preventive services and treatment of chronic diseases were free of charge.
4. Accessibility of highly qualified medical services to socially underprivileged and unprotected segments of the population is a problem that could be solved in part by exempting them from payment while requiring fellow citizens with higher incomes to pay for such services.	4. Retirees, veterans, disabled persons, expectant mothers and children up to 15 years old were usually exempt from payment for medical services rendered.

As is evident from this comparison, the world experience of using a system of paid medical services for the most part confirms the results of introducing self-financing in South Kazakhstan Oblast.

We drew up and proposed the "Standard Program for Introducing Paid Health Services" on the basis of the results of the ongoing experiment in this direction.

Standard Program for Introducing Paid Health Services to the Population in South Kazakhstan Oblast

1. Mandatory payments for health services shall be made only by residents who are unable to pay; the underprivileged and poor shall be exempt from payment.

2. The shared-risk funding system (an insurance system for example) shall cover the expenses of rendering unforeseen high-cost services.

3. Preventive services shall be rendered and infectious diseases shall be treated free of charge, or for a minimum fee.

4. Additional financial resources received in payment of health services shall be used to upgrade the quality of health services.

5. The fees for health services shall be consistent with the costs of these services.

6. Medical institutions receiving income in the form of fees for rendered services shall use the larger part of the profit (and possibly all of the profit) in two ways:

to replenish the reserve of medications;

as an additional source for material incentives to associates.

7. Representatives of the public shall supervise the activity of the directors of medical institutions pro-

viding paid services (they shall monitor cash deposits and use of earned monetary resources).

8. Part of the earned monetary resources may be contributed to a fund subsidizing medical institutions operating in places where income is low (unstable) or the population density is low.

A comparative analysis made with advice from the leadership of the "Health Reform" program shows that paid services provided in Shymkent, their list, and their volume correspond to items 1, 3, 4, 5 (in part) and 6 of our standard program.

In accordance with provisions of item 2, shared risk will become an integral component of the oblast's mandatory health insurance program for 1995 in Shymkent. This will make it possible to protect users of paid health services when it comes to paying for high-cost services required in the treatment of certain diseases.

Concurrently we need to improve public supervision over use of monetary resources received for paid health services (item 7), since such supervision is practically nonexistent today.

Item 8 of the standard program is important: It allows subsidies to be paid under the paid health service system to public health institutions operating in places known for their low income levels or a low population density.

Thus medical institutions of the health department serving as the main objects of the experiment successfully introduced a self-financing mechanism with a certain amount of assistance from the "Health Reform" program. In the course of implementing the mandatory health insurance program, we need to devote due attention to introducing payment taking the form of deductions or joint payments, to be made as compensation for health services rendered.

In order to support broad introduction of the system of paid health services the RK Ministry of Health drew up a package of documents entitled "Problems of Financing Public Health Under the Conditions of Market Relations" as a way of establishing a legal foundation. This package was submitted to the country's Cabinet of Ministers for consideration.

Our experiment showed that public health institutions should be granted the right to establish funds for production and social development and for labor compensation out of budget resources and supplementary financing sources (paid services, agreements with enterprises, medical insurance resources etc.).

This package of documents includes the interim statute "On the Conditions and Procedure of Rendering Paid Health and Preventive Services in State Public Health Institutions," according to which paid health service departments (offices) providing paid medical, social and health improvement services to the public are to be created in order to satisfy more fully the public's demand for highly qualified health care, and allow free choice of a specialist by the patient. In this case health care and social assistance are to be granted regardless of the applicant's place of residence and place of work.

The indicated paid health care subdivisions are to independently plan their activity and determine the prospects for development on the basis of the demand for services.

One final thing. Paid health service departments (offices) are to be organized on the basis of special resources under state public health institutions supported by the state budget, with the permission of public health agencies. Concurrently, such subdivisions are to be exempt from collection, as budget income, of the amount by which income exceeds expenses according to estimates of special resources needed for development and reinforcement of the material and technical base.

Kazakhstan: State of Rural Public Health

964D0774B Almaty ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian Aug 95 No 8, pp 8-12

[Article by I. A. Anambayev, Republic of Kazakhstan Ministry of Health; UDC 614.2:362.1(547-202)

[FBIS Translated Text] Health support is being provided to rural inhabitants in accordance with the laws "On Safeguarding the Health of People in the Republic of Kazakhstan" and "On the Developmental Priorities of the Village, Town and Agroindustrial Complex in the Kazakh SSR."

Rural public health is presently represented by 7,452 therapeutic and preventive institutions, to include 4,980 FAPs [paramedic-obstetric stations], 2,061 medical outpatient clinics and section hospitals, and 236 TsRBs [central rayon hospitals] and rayon hospitals.

Moreover specialized quality health care is provided by over 160 oblast therapeutic and preventive institutions.

There are 292 mobile medical outpatient clinics, and stomatological and fluorographic facilities and laboratories for inhabitants of remote rayons and persons employed in distant-pasture livestock farming. There are 79,687 hospital beds and 2,452 day hospital beds at the rural level.

Presently 15,586 physicians and 71,861 secondary medical workers are employed in rural administrative regions. Health care is provided in 14-30 medical specialties in rayon and oblast hospitals. Eighty-five public

health facilities were built and placed in service in the last 4 years in rural areas, to include 8 TsRBs, 9 SUBs [rural section hospitals], 47 SVAs [rural medical outpatient clinics] and 21 FAPs.

At the same time rural public health continues to lag far behind the urban level. The material and technical base of medical institutions is extremely weak. New construction is practically nonexistent today. Rural therapeutic and preventive institutions are inadequately supplied with medical equipment and apparatus, and the qualifications of rural medical personnel do not always meet the requirements. There are now more than 1,000 small population centers in the republic without medical institution of any kind, or even a medical worker. One out of every five TsRBs (22 percent), 70 percent of SUBs, and 92 percent of SVAs and FAPs are housed in makeshift, crowded premises, while the premises of some of them are dilapidated.

A significant number of these institutions do not have hot water, and they use stove heating. More than 50 percent of FAPs lack telephones, and many of them do not have refrigerators. Overall, more than 200 SUBs and SVAs do not have ambulances. Two hundred sixty-nine SUBs and SVAs are working without a single physician; there is not even a secondary medical worker in 274 FAPs.

There are great difficulties in providing medical personnel for rural inhabitants. Around 350,000 townspeople receive practically no medical care at their place of residence.

As of today, rural administrative regions are short 2,500 physicians and 7,000 secondary medical workers. High turnover of personnel is noted due to low wages and other unfavorable socioeconomic and personal factors. For example 121 physicians and 392 secondary medical workers left Kokchetav Oblast, 242 and 862 left Taldy Kurgan Oblast, 179 and 912 left South Kazakhstan Oblast, 65 and 262 left Kustanay Oblast, 53 and 217 left West Kazakhstan Oblast, and respectively 43 and 24 left Turgay Oblast.

The average wages of medical workers were 763 tenge in Kzyl Orda Oblast, 965 in Aktyubinsk, 891 in Almaty, 1,001 in East Kazakhstan, 995 in Atyrau, 918 in Dzhambul, 1,006 in Zhezkazgan, 1007 in Karaganda and 1,133 in Kokchetav oblasts. The average wages of physicians and secondary medical personnel were respectively 1,492 and 885 tenge in Pavlodar Oblast, 2,200 and 998 tenge in North Kazakhstan Oblast, 1,878 and 920 tenge in Semipalatinsk Oblast, 1,963 and 871 in Taldy Kurgan Oblast, 1,857 and 955 in Turgay Oblast, 2,138 and 1,072 in West Kazakhstan Oblast, 696 and 450 in Akmola Oblast, and 1,652 and 969 tenge in South Kazakhstan Oblast.

Wages were paid late in all quarters of 1994 in all oblasts.

The republic's budget deficit also affected the financing of rural public health. In 1994 only 36-75 percent of the annual needs of rural therapeutic and preventive institutions were financed.

Therapeutic and preventive institutions were financed in 1994 in relation to only three items (wages, food, medications), and with a great delay.

The health of the rural population, which makes up 43 percent of the republic's total population, is clearly unfavorable today. Demographic indicators are worsening. This includes a decrease in the birth rate and shortening of the average life span. The population's rate of natural increase is tending to decrease, and overall morbidity among children and adults grew by a factor of 1.5 in the last few years, chiefly due to an increase in oncological, cardiovascular, nervous, mental, respiratory and digestive tract diseases.

The occurrence of chronic nonspecific illnesses, which up to 45 percent of inhabitants suffer, is high in the rural population.

For every 1,000 persons subjected to comprehensive medical examinations, 551.1 additional cases of disease are revealed for which the people had not applied for medical assistance. In rural areas lacking treatment and rehabilitation facilities, chronic diseases are becoming the most important socioeconomic problem.

The level of primary disability in rural areas exceeds the republican indicator by a factor of 1.5. According to data of several scientific studies one out of every three men and one out of every five women in rural areas do not live to retirement age. In addition to overall mortality, infant mortality remains high in the countryside. Growth of missed cases of oncological and other chronic diseases has been noted. A large proportion of rural inhabitants begin and end their treatment with paramedics. This is evidence of insufficient development of specialized forms of health care in rural areas. Another cause is the growing cost of transportation, which significantly limits access of rural inhabitants to qualified and specialized health care.

Worsening of health is aggravated by the unsatisfactory ecological situation, dramatic growth of prices of staples and their shortage, and deficiencies in supplies of clean drinking water.

Children make up 32 percent and women of childbearing age make up 25 percent of the age structure of

the republic's population. Thus the contingent requiring special concern of the state comprises over half of the population, with this contingent being even larger in the countryside. Deeper research showed that the health of women and children living in rural areas is significantly worse than of those living in cities. Their health index is around 20 percent, one out of every two expectant mothers suffers anemia, one out of every five suffers kidney diseases, and one out of every 10 suffers cardiovascular diseases. Up 60-80 percent of women who die due to complications of pregnancy, childbirth, and the postnatal period live in rural areas, and one out of every three of these has had children in the past. Morbidity and mortality is high among newborn infants. Rural children are significantly behind their urban peers in physical development owing to shortcomings in organization of children's nutrition, and an imbalance in the main components of the food ration—a shortage of amino acids, vitamins and minerals. Kazakhstan does not have its own baby food industry, and shops have not been organized for baby food production. Sour-milk products for children are made only in dairy kitchens, the number of which is decreasing dramatically. In rural areas they occupy ill-suited premises, they are not mechanized, around 30 percent of them are closed today, and the same percentage are working with interruptions due to absence or late deliveries of high quality milk. The product assortment is limited to one or two items (boiled milk, kefir), the output of which satisfies 26 percent of the demand.

Providing good drinking water to the public remains one of the most important hygienic problems, because bacterial contamination of water is the leading factor responsible for the high incidence of intestinal infections. An inspection of the sanitary and technical condition of water mains confirmed the presence of many cases of gross violation of public health norms and a failure to observe the "Rules of Technical Operation of Water Supply Systems of Population Centers." Centralized water supply is available to only 52 percent of the rural population of the republic, 18 percent of Kzyl Orda Oblast, 32 percent of West Kazakhstan Oblast, 31 percent of Semipalatinsk Oblast and 31 percent of Atyrau Oblast.

Water supply facilities and networks are kept in service in many rural population centers until complete breakdown, and they are not flushed out or decontaminated.

Of the 2,462 rural water pipelines, 17.6 percent do not meet public health requirements. While the proportion of bacteriologically substandard samples is 5.1 percent in the republic, it reaches 30 percent in rural settlements of Kzyl Orda, Kokchetav, Kustanay, Taldy Kurgan, Dzhambul and South Kazakhstan oblasts, and in certain population centers it reaches 70-100 percent.

The epidemiological situation in the Republic of Kazakhstan has been unfavorable in relation to tuberculosis over the course of many decades.

In the last 2 years a number of indicators have been observed to worsen, chiefly in regions where susceptibility to tuberculosis is high. Interruptions in the supply of X-ray and fluorographic film, BCG vaccine and tuberculin, drugs and disinfectants have significantly affected the conduct of preventive measures and treatment of tuberculosis in the republic as a whole.

The proportion of the population receiving medical examinations decreased to 51.7 percent in 1991-1993. The effectiveness of preventive examinations is falling. As a result 45 percent of patients with active tuberculosis are revealed upon their application to a polyclinic. Owing to this, the number of cases of destructive tuberculosis is growing among first-time patients. Detection of sick children with destructive forms of tuberculosis is raising alarm. This percentage was 1.7 for the republic as a whole. This indicator is high in Atyrau, West Kazakhstan, Kzyl Orda, Taldy Kurgan and Turgay oblasts owing to a decrease in the proportion of newborn infants receiving vaccinations and revaccinations. The incidence of tuberculosis is high among agricultural enterprises in several oblasts. Tuberculosis is detected among livestock workers at a rate four times higher than in the rest of the population.

The brucellosis situation is unfavorable. In 1992-1993 there were 5,490 patients, and there were 2,982 in 1994. This indicator was 17.7 cases per 100,000 population in the republic as a whole in 1994, and it was 51.7 in Dzhambul Oblast, 54.2 in Almaty Oblast and 31.0 in South Kazakhstan Oblast. From 83.5 to 92 percent of all morbidity is in the rural population.

The reasons for the high incidence of brucellosis in the population include numerous violations of veterinary and public health regulations, late detection and isolation of sick animals, maintenance of sick animals at farms for too long a time, and poor veterinary and public health practices in peasant farms.

The situation regarding health services and protection of the labor of livestock workers, especially on distant pastures, is becoming serious in the republic.

Not a single farm has a mobile paramedic station supplied with modern medical equipment. Even paramedics assigned to provide health services to workers in distant-pasture livestock farming and their families often work without transportation, making do with whatever transportation happens to be available.

Proper support to the work of mobile medical teams and of fluorographic and stomatological facilities is important to the prompt revelation and treatment of diseases among livestock workers.

Unfortunately these medical forces and resources experience periods of idleness or work unproductively because of the absence of fuel, lubricants, and spare parts. Farm directors do not ensure timely medical examination of all livestock workers and their families and their subsequent quick recovery.

Because of late vaccination of agriculture animals against anthrax and unsupervised forced slaughter, cases of anthrax are recorded among people in population centers each year. Twenty-four persons got sick in 1993 (25 in 1992). Cases of illness were recorded in farms of South Kazakhstan (11), Aktyubinsk (4), Almaty (4), West Kazakhstan (3) and Turgay (2) oblasts.

Bath services to the rural population are unsatisfactory, with the availability of bathing places being less than 50 percent of standard. Baths are being shut down in many towns as being unprofitable, while ticket prices have significantly risen in those still in operation, making them inaccessible to poor segments of the population. The availability of bath services is especially low for the rural population of Semipalatinsk, Dzhambul and Aktyubinsk oblasts—10-15 percent. The sanitary and technical condition of baths worsened dramatically in recent years. Practically all baths of Kellerovskiy Rayon in Kokchetav Oblast, and a large part of them in Atyrau Oblast's Kurmangaliyevskiy and Embinskiy rayons, Semipalatinsk Oblast's Abayskiy Rayon, Almaty Oblast's Balkhashskiy, Kegenskiy and Raimbekovskiy rayons, North Kazakhstan Oblast's Zhambylskiy Rayon and East Kazakhstan Oblast's Tarbagatayskiy Rayon are in dilapidated state.

Taken altogether, the yearly decline in availability of baths to the rural population, the absence of the needed quantity of medical checkpoints and the acute shortage of equipment, detergents and disinfectants are promoting high incidence of scabies and the spread of pediculosis.

For example the incidence of scabies increased in 1994 by a factor of 1.8 compared to 1993, to a level of 232.6 per 100,000 population, as compared to 132.1.

The highest indicators in 1994 compared to 1993 were noted in East Kazakhstan—636.7 (200.8), Semipalatinsk—534.3 (230.2), Atyrau—421.4 (272.4), Mangistau—420.3 (237.8), and North Kazakhstan—374.0 (162.2) oblasts.

The infectious disease situation remains unstable in the rural population. The incidence of bacterial dysentery increased 7.2 percent in 1994 compared to 1993. Morbidity is highest in East Kazakhstan (1993—116.9; 1994—245.0), Pavlodar (132.7 and 146.3), Mangistau (99.7 and 135.8) and Semipalatinsk (85.2 and 117.5) oblasts, as compared to republican indicators of 91.1 and 97.6 respectively.

Despite the decrease in incidence of viral hepatitis in the republic as a whole, its growth is observed in Aktyubinsk, Dzhambul, Zhezkazgan and Mangistau oblasts, and its level remains high in Almaty, South Kazakhstan, Kzyl Orda and Taldy Kurgan oblasts.

The vaccine supply situation grew dramatically more complex since 1993. The republic does not have a single enterprise producing vaccines, and it depends completely on CIS countries. Moreover the cost of vaccines grew by several hundred times, which created major payment difficulties. The demand for the main types of vaccines was 30 percent satisfied in 1993, and 40-50 percent satisfied in 1994. Immunization was carried out chiefly owing to deliveries of vaccines along the lines of humanitarian assistance, and these vaccines were used only to immunize children. Adults remained unimmunized against "controllable infections" in 1993-1994.

All of this had a negative effect on infectious morbidity. The incidence of diphtheria grew from 82 cases in 1993 to 489 in 1994. Large outbreaks of diphtheria were recorded in many oblasts, and mortality grew dramatically—from three cases in 1993 to 27 in 1994.

Measles infection continues to be recorded at a high level.

There have been no official statistics on rural public health since 1987, as a result of which it is impossible to make any efficient analyses or take effective steps to improve the position of rural public health. Practically no comprehensive scientific research is being conducted in the countryside.

On the whole, the health of the rural population is in a woeful state. Given the financial situation that has recently established itself in rural public health, immediate steps must be taken to make more effective use of available resources.

At the same time the work of rebuilding hospitals and putting hospital beds to new uses is slow in Taldy Kurgan, Dzhambul, Atyrau, Almaty, South Kazakhstan and other oblasts. Despite the fact that large numbers of beds remain unfilled or are used ineffectively, and budget appropriations are acutely short, executives are failing to take immediate steps to reorganize rural section hospitals into rural medical outpatient clinics offering day hospital facilities, or to create nursing

hospitals and departments and rehabilitative treatment departments, the cost of which is significantly lower.

On the average, for example, one bed was not used for more than 105 days in 1993 in Taldy Kurgan Oblast's Taldykorganskiy Rayon, and around 100 days in this oblast's Kerbulakskiy and Alakulskiy rayons. An average of 137 beds were not used over the course of 1993 in Atyrau Oblast's Zhylyoyskiy Rayon.

The effectiveness with which beds of remote rural section hospitals are being used is very low. Examples include the SUB of the town of Zhylandy, Uygentasskiy Rayon (42.8), the Koktum SUB in Alakulskiy Rayon (103.1) and the Zhanatalap SUB in Karatalskiy Rayon (126.3) of Taldy Kurgan Oblast, the Tanday SUB in Makhambetskiy Rayon (94.1) and the Damba SUB in Balykshinskiy Rayon (185.7) of Atyrau Oblast, and certain section hospitals of Sverdlovskiy and Zhualinskiy rayons (106-186 days) of Dzhambul Oblast. A similar situation is evolving in many other oblasts.

In population centers where health care is rendered by secondary medical workers, their diagnoses are not accounted for statistically, which naturally has a negative effect on the true morbidity indicators of the population, and correspondingly affects determination of the need for budget appropriations.

This situation could be rectified by organizing mobile forms of health care to the population, rendered by medical personnel freed from hospitals in which beds are used ineffectively.

Oblast health administrations and institutions subordinated to them are introducing new forms of organization of health care for the rural population too slowly. Real possibilities and reserves for making the bed fund work effectively in rural areas, and for reorganizing use of beds in a new way to enhance primary medical and public health assistance are weakly utilized.

Extremely insufficient and late financing, the absence of budget operations for further development of the material and technical base of rural therapeutic and preventive institutions, and poor supply of medical apparatus, equipment, motor transportation, tools, expendables, medications and vaccine preparations to them remain the main problems of the republic's rural public health.

The republic lacks a unified system of views on the problems of privatization and conversion of rural therapeutic and preventive institutions into joint-stock companies, although most oblast health departments oppose such a move.

The Main Administration for Therapeutic and Preventive Care finished its work jointly with the Scientific Center for Medical and Economic Problems of Public Health of the Kazakhstan Republic Ministry of Health on the scientific research topic "Social, Hygienic and Economic Aspects of Organizing, Planning and Managing Rural Public Health Under the New Conditions" intended for 1995-1996.

These data point to the need for implementing a number of purposeful state measures to improve rural public health and carry out medical measures. To be specific:

hastening creation of day hospitals, nursing hospitals and departments, and restorative treatment in rural areas out of ineffectively used beds. Organizing day hospitals at all TsRB, SUB and SVA polyclinics;

developing mobile forms of medical services more extensively, creating regular mobile medical teams for these purposes out of resources economized by putting the bed fund to new uses;

improving the supply of medical equipment, apparatus and drugs to rural therapeutic and preventive institutions;

introducing official statistics characterizing rural public health indicators into the statistical reporting by the RK Ministry of Health;

having oblast health administrations attach priority during certification to rural physicians and secondary medical workers, especially in remote regions, and make a practice of certifying medical workers in remote regions using traveling boards;

recommending to the directors of the Farmatsiya (OPU) [not further identified] and the Meditekhnika (OPTU) [not further identified] that they take whatever steps possible to reduce the cost of drugs and medical equipment by means of their internal reserves;

recommending establishment of funds under oblast and rayon administrations to maintain the supply of drugs for the population;

ensuring timely financing of therapeutic and preventive institutions of rural public health in the amount needed to provide the necessary volume of preventive, therapeutic and economic measures;

foreseeing planned scientific research (for a period of 2-3 years) aimed at reforming rural public health in its diversity. Providing for the soonest possible creation of the grounds for a transition to per-capita financing in rural areas;

establishing that the frequency of visits by the rural population to FAP secondary medical workers must be included in the morbidity indicator for this group of residents.

having the chiefs of oblast health administrations implement measures to sensibly locate and effectively utilize existing public health institutions in rural rayons;

acknowledging that absence of resources with which to acquire vaccines of the needed assortment and quantity will lead to uncontrollable growth of infectious diseases among children;

acknowledging that despite the highly complex economic situation in the Republic of Kazakhstan, the problems of at least minimally balanced nutrition for children in rural areas are not to be removed from the agenda. Opening baby food shops (departments) under city (rayon) dairies and fruit and vegetable (meat-packing) plants;

reviewing the wages of rural medical workers, and raising them to the level of specialists in the leading sectors of the national economy.

Kazakhstan: Fleas of the Great Gerbil as Vectors of Listeriosis Infection in the Prikapchagayskiye Muyunkumy

964D0774C Almaty ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian Aug 95 No 8, pp 43-44

[Article by A. O. Sheykin, V. M. Stepanov, L. Yu. Lukhnova, O. S. Serzhanov and T. V. Meka-Mechenko, Kazakh Antiplague Scientific Research Institute, Almaty; UDC 599.323.4.576.895.775.616.98:579.869.1(574.5)]

[FBIS Translated Text] **Abstract: Great gerbil colonies were discovered in sandy places during a survey of the Muyunkumy Desert along the Ili River. Fleas infected with listeriosis microbes were discovered on trapped gerbils. When these fleas were experimentally released on white mice, transfer of listeriosis to the animals was noted. The mice died on the 10th day, and the initial *Listeria* culture was isolated from their livers.**

Bibliography: 5 references

Key words: listeriosis, transmission of listeriosis from gerbils to other animals

Great gerbils are rodents widely distributed in deserts of Central Asia and Kazakhstan. Being the main plague carriers in these regions, they can fall ill themselves, and infect man and other animals with infectious diseases not very well known by doctors in practical public health. One such diseases is listeriosis—an infection evoked by the microbe *Listeria monocytogenes*. Listeriosis is expressed in man by diverse clinical manifestations that could easily be taken for diseases of other etiology. Its clinical symptoms include signs of influenza, general septic infection, nervous disorders, angina with the participation of lymph nodes and monocytosis, and local inflammations of mucous membranes. Listeriosis can be diagnosed with certainty in a living patient only by bacteriological analysis [5].

We discovered thriving great gerbil colonies 26 km north of the city of Kapchagay, on the left bank of the Ili River, during field work in the Prikapchagayskiye Muyunkumy. The possibility of their penetration to this region was pointed out earlier in [2]. The active Taukum independent plague focus is in direct proximity to this place (15-20 km) [4], and there are a number of population centers, herdsmen campsites and troop practice ranges in the surveyed area, which is also frequented by hunters, fishermen and tourists. Nomadic herdsmen pass through this desert, and camels having direct contact with ectoparasites of the great gerbil in its habitat graze here. The burrows of the great gerbil are practically continuous along the desert edge (heli-type colonies). Their number decreases within the desert proper, dropping to 0.3-0.6 per hectare. A sizable quantity of ixodid ticks of genera *Hyalomma*, *Haemaphysalis*, *Dermacentor* and *Rhipicephalus* were revealed in the colonies. The index of abundance of fleas on the gerbils—of "fur fleas"—was 38. Samples collected from the rodents were dominated by the flea *Xenopsylla hirtipes*—40 percent. The indicators for migrating fleas are significant—250-300 specimens per colony, and it is known that fleas of the great gerbil actively attack and bite man [3].

For our research, we caught 10 great gerbils from different colonies and dug up 20 of their colonies to collect ectoparasites. The following flea species were discovered in the laboratory from combed gerbils: *Xenopsylla gerbilli minax*, *X. hirtipes*, *Echidnophaga oschanini*—active vectors of various micro-organisms [1]. These insects play a significant role in their natural circulation, and the existence, established earlier, of contact between the gray rat, which inhabits the Kapchagay vicinity, and the great gerbil does not preclude the possibility of exchange of ectoparasites between them.

The fleas were analyzed individually bacteriologically. The microbe *Listeria monocytogenes* was isolated from three seedings from *X. hirtipes* fleas. The microbe grew in the form of tiny dewdrop colonies on Hottinger agar (pH 7.2) to which 3 percent hemolyzed blood was added. Clouding, followed by settling of a precipitant at the bottom of the test tube, was discovered in Hottinger broth after one day of incubation at 28°C. There were thin Gram-positive rods in the smear. Catalase activity was noted in the strain, and it was observed to reduce methylene blue. The isolated culture ferments to form gas-free acid glucose in aerobic and anaero-

bic conditions, maltose, rhamnose, salicin, esculin and, slowly, glycerin (on the fifth day); it does not reduce nitrates into nitrites; it does not ferment arabinose, mannitol, sucrose, dulcite and raffinose; it does not form indol and hydrogen sulfide; the micro-organism is mobile at room temperature, it possesses hemolytic activity (a small zone of incomplete hemolysis), and it does not liquefy gelatin. The *Listeria* culture agglutinates to the titer of antilisteriosis serum, and it falls under the first serovar. Decelerated enzymatic activity, which was restored after several subinoculations on Martin agar, was a unique feature of this *Listeria* strain.

Seeding of organs of great gerbils on Hottinger agar produced a negative result.

Because the question as to natural reservoirs of listeriosis infection and as to the role of vectors remains debatable, we experimentally infected the fleas *Xenopsylla cheopis* and *X. gerbilli minax* with the isolated microbe *Listeria monocytogenes*. Infection was accomplished by the known procedure on a biological membrane using defibrinated rabbit blood containing 300,000 microbial colonies of the investigated strain. Over half of the fleas were infected. The fleas maintained the *L. monocytogenes* strain alive for 12 days from the moment of their infection when maintained at a temperature of 18-20°C. When fleas infected with *Listeria* were released on white mice, transfer of the infection to these animals was noted in two out of 13 cases. The mice died on the 10th day after infection. The initial culture was isolated from their liver and spleen.

Thus our field survey of a parcel 26 km north of the city of Kapchagay, on the left bank of the Ili River, near population centers, established the abundant presence of the great gerbil on this territory, high infestation of the gerbils by fleas, contact with the gray rat, and possible exchange of ectoparasites between them. A virulent *Listeria monocytogenes* culture that causes listeriosis in people and domesticated animals was isolated from fleas on the great gerbil.

In order to combat listeriosis, medical workers must be aware of this infection, and public health education should be conducted among people residing in this territory. A conclusive diagnosis of this disease can be made only upon obtaining bacteriological confirmation from the Kazakh Antiplague Scientific Research Institute.

Bibliography

1. Vashchenok, V. S., "Blokhi—perenoschiki vozbuditeley bolezney cheloveka i zhivotnykh" [Fleas—Vectors of Human and Animal Disease Agents], Leningrad, Nauka, 1988, 166 pp.

2. Karpov, A. A., Pole, S. B. and Solovyev, M. M., "Previously Unknown Great Gerbil Colonies on the Middle and Lower Reaches of the Ili River," in "Peschanki—vazhneyshiye gryzuny aridnoy zony SSSR. Materialy III Vsesoyuznogo soveshchaniya. Tashkent, 19-23 sentyabrya 1989" [Gerbils—The Most Important Rodents of the Arid Zone of the USSR. Proceedings of the Third All-Union Conference. Tashkent, 19-23 September 1989], Tashkent, FAN, 1989, pp 51-52.

3. Lukhnova, L. Yu., Aykimbayev, A. M., Serzhanov, O. S. and Sheykin, A. O., "Capability of *X. g. minax* Fleas for Attacking Man and Feeding on His Blood," ZDRAVOOKHRANENIYE KAZAKHSTANA, No 6, 1993, pp 17-18.

4. "Rukovodstvo po landshaftno-epizootologicheskomu rayonirovaniyu prirodnykh ochagov chumy Sredney Azii i Kazakhstana" [Handbook of Landscape and Epizootological Zonation of Natural Plague Foci of Central Asia and Kazakhstan], Almaty, 1990, 29 pp.

5. Tripolitova, A. A. and Borisova, G. V., "Listerioz" [Listeriosis], Tomsk, 1965, 258 pp.

Kazakhstan: Effect of the Production Environment on the Health of Workers of the Pavlodar Chemical Plant

964D0774D Almaty ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian Aug 95 No 8, pp 44-46

[Article by M. Ye. Kulmanov, V. L. Reznik, R. I. Semenova, T. I. Slazheva, A. K. Shulanova, K. N. Dzhulanova, N. Ya. Yakovleva, G. A. Butrin and N. N. Leontyev, Kazakh Institute for Advanced Training of Physicians, Almaty; Tsentr Okhrany Zdorovya MGNVP, Khimprom MSCh PO, Pavlodar City Public Health and Epidemiological Station; UDC 613.632:313.131]

[FBIS Translated Text] **Abstract: A complex mixture of substances in air of the work zone affects the bodies of workers at enterprises of chemical industry. This situation is also typical of the Pavlodar Chemical Plant. In addition to studying the working conditions, a thorough analysis was made of morbidity involving temporary incapacitation, and thorough medical examinations of workers of different production operations were carried out. Significant peculiarities of morbidity involving temporary incapacitation were established, as was the relative importance of particular diseases in pathology revealed in medical examinations depending on the specific conditions of the production environment and time of work in the given production operation.**

Key words: chemical plant, production environment, formation of morbidity.

The production environment is known to be one of the leading environmental factors affecting human health. This can manifest itself to the greatest degree at enterprises of chemical industry, where the air of the work zone is contaminated as a rule by some toxic substance, and most often by a complex mixture of these substances.

Air in the work zones of different production operations and shops of the Pavlodar Chemical Plant may contain mercury, chlorine, antimony trioxide, lead, phosgene, hydrogen chloride, hydrogen fluoride, polyvinyl chloride, phenol, phenolformaldehyde, ethylene glycol, hydrogen sulfide, sulfuric anhydride and other inorganic and organic substances. The compositions of mixtures contained in the air of different shops differ significantly, and the actual concentrations of many of the substances often exceed permissible limits. Thus according to data of the departmental laboratory the mercury concentration in air of the work zone of the filtration and dechlorination division (shop No 2) exceeded the PDK [maximum permissible concentration] in 50 percent of the samples, and in shop No 3 (the electrolysis bay) the chlorine concentration is above the PDK in 39.3 percent of samples at elevation 0.0 and 85.6 percent of the samples at elevation 4.8. According to observations in 1990-1992 the concentration of metallic mercury vapor in air at this same elevation was above the PDK in 92-100 percent of the samples. In shop No 5 (blending division) the lead concentration was above the PDK in 7.7-66.7 percent of air samples. The dust concentration in the polyvinyl chloride suspension batching division was above the PDK in 60.1-71.2 percent of analyzed air samples. It would be natural to suppose that such working conditions affect the bodies of the workers and, in turn, their health and the indicators for morbidity involving temporary incapacitation.

The goal of our investigation was to establish the peculiarities of formation of morbidity involving temporary incapacitation, and to assess the health of workers in different production operations of the Pavlodar Chemical Plant in connection with the possible effects of working conditions.

In order to achieve our goal we made a meticulous analysis of morbidity involving temporary incapacitation over a period of 3 years focusing on year-round workers, and we organized thorough medical examination of 1,146 workers, including 615 men and 531 women, with the help of leading specialists. All subjects were divided into six groups depending on the characteristics of the production environment: the first—persons working in the presence of mercury and its compounds, including in cases of combined action of mercury with other substances; the second—persons working in the presence of chlorine and its compounds, including in combination with substances other than mercury; the third—persons working in the presence of polyvinyl chloride and other organic compounds; the fourth—workers of other main production operations; the fifth—workers of auxiliary production operations; the sixth—a control group (water supply shop, trolley shop, security, etc.)

In addition all workers were differentiated by time of service: A—up to 5 years, B—5-10, C—over 10 years of work in the given production operation.

Morbidity analysis established that in 1990, the indicator of the number of persons falling ill per 100 workers, which is considered to be one of the most informative, was 46.9 +/- 1.45 percent plant-wide in group A, growing to 51.7 +/- 1.81 percent in group B ($P<0.05$), and once again decreasing to 45.7 +/- 2.02 percent in group C. The same pattern is observed in 1991, with the respective indicators being 48.8, 53.2 and 51.0 percent. In this case the differences in the number of cases of illness per 100 workers were even more pronounced, and this indicator reaches the following values in 1990 [sic] in group A—100.4 +/- 2.5, B—139 +/- 4.28 ($P<0.05$) and C—114.8 +/- 4.35 ($P<0.05$ when compared with groups A and B), and in 1990—107.2 +/- 3.29, 136.9 +/- 4.39 ($P<0.05$) and 127.3 +/- 4.29 ($P<0.05$ when compared with group A).

It should be noted in this connection that some of the peculiarities of formation of morbidity involving temporary incapacitation in the plant are, according to the criteria of the adopted classification, the very low and low morbidity as determined from the number of persons falling ill, and the above average and high indicators in relation to the number of cases of incapacitation.

In terms of the number of cases of incapacitation per 100 workers, morbidity is characterized as high in groups A and B, while in group C it is average in 1990 and above average in 1991. Thus, in 1990 it was 1,256 days in group A, 1,248 in group B, and 842 days in group C, while in 1991 the figures were 1,344, 1,259 and 1,084 days respectively.

An analysis of the described data generally turns one's attention to the fact that the indicators for the group with a time in service of 5-10 years are higher than for persons who worked less than 5 years, and to the fact that the indicators for group C were lower than those in group B. We associate such dynamics with the doubtless effect of harmful working conditions on the bodies of the workers and their subsequent arbitrary selection for work in particular production operations of the plant.

This is consistent with data of the medical examinations, and particularly with indicators obtained on their basis for the rate of occurrence of disease (per 100 examined workers of the given occupational and time-in-service group) in relation to each of 17 disease classes of the MKB-9 [not further identified], and with the structure of the revealed pathology.

Certain differences in the structure of revealed diseases in relation to disease classes are typical, as may be deduced for example from the overall pattern for groups of men and women employed in different production operations and working 10 years or more. Also typical in this case are some general patterns in relation to classes III, V, VI, IX and XIII.

Differences in the structure of revealed diseases in persons working more than 10 years are most highly pronounced in all groups differentiated with respect to production conditions. In this case from 34 to 50 percent of the diseases making up the revealed pathology are of digestive organs. Among persons working in the presence of mercury, the share of diseases of the endocrine system, nutritional disorders, and metabolic and immunity disturbances is significantly greater within the structure of revealed diseases than in other groups (18.7 percent as opposed to 4.6, 1.5, 3.8, 8.2 and 8.2 percent in the second through sixth groups); the corresponding figures for mental disorders were 11.6 percent as opposed to 1.2, 0.6, 1.9, 2.4 and 2.8 percent. In the first group these classes of diseases hold second and third places among all revealed diseases. Diseases of the nervous system and sensory organs occupy second place in the structure in the second group. This group of diseases is also typical of persons working in the presence of polyvinyl chloride and organic compounds, as well as workers of other main and auxiliary production operations. This indicator is somewhat lower in the control group.

All of this is fully consistent with published data on the effects of toxic substances in the air of production spaces. At the same time in our opinion the relatively high proportion of diseases of the nervous, urogenital and skeletomuscular systems in the control group is associated on one hand with transfer of sick individuals to work in less-harmful production operations, and on the other hand with the lower requirements regarding medical contraindications against hiring for work in these shops. Random selection also plays a certain role.

Changes in the proportion of the indicated classes of diseases in the overall structure of diseases revealed by medical examinations in different time-in-service groups of men also provide evidence of the doubtless effect of harmful factors of the production environment (the first, second, third, fourth and sixth groups) on the health of the workers.

Thus, the share of diseases pertaining to class III is 7.4 percent in group 1A, 15.3 percent in 1B, and 24.9 percent in 1C. Growth of the proportion of these illnesses with increasing time in service is also characteristic of the second and third occupational groups. The levels are stable in the control group, which confirms our earlier hypothesis. The time-in-service dynamics for diseases of class V (mental disorders) in the first group are similar to those described.

Diseases of the nervous system and sensory organs (class VI) among workers with time in service from 5 to 10 years in the second occupational group represent 21.5 percent of the total number of diseases in this group. Diseases of this class comprise 20.7-23.1 percent in different time-in-service groups for the third occupational group, which is fully consistent with the peculiarities of the biological action of organic substances

There are also certain differences in the structure of diseases revealed in men and women. In particular the share of diseases of the urogenital system (class X) is relatively high among women. For example the proportion of these diseases in different occupational groups with time of service greater than 10 years is 9.3-16.4 percent for women and from 0 to 2.4 percent for men. However, the highest share of the indicated diseases is in women's groups with a time in service up to 5 years (19.4-33.3 percent). We believe that this situation is associated with significant occurrence of the noted pathology when women are first hired for work. Later on, the disease progresses or develops in less-resistant women in the harmful working conditions, after which some of the women are let off while others are treated, and they recover.

Preliminary research results permitted the following general conclusions:

The working conditions of workers in the main production operations have a significant effect on their health, which makes it possible to define the production environment as being unfavorable from a hygienic point of view;

working conditions and the nature of the work process of workers in the main production operations and occupations must be subjected to special study at the appropriate level, and the harmfulness, heaviness and stressfulness of their work must be subjected to hygienic evaluation;

a scientifically substantiated complex of recommendations for optimizing working conditions and improving the health of workers needs to be developed;

purposeful work to prevent diseases that are most significant in the structure of revealed pathology must be conducted on priority, and revealed patients must be treated.

Problems of Certifying Drugs and Medical Products in the Republic of Kazakhstan in the Present Stage

964D0774E Almaty ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian Aug 95 No 8, pp 56-59

[Article by A. A. Abdrakhmnov, E. M. Bisenbayev and R. N. Dzhilikbayeva, Medstandart State Scientific-Practical Certification Center, Almaty; UDC 615.45]

[FBIS Translated Text]

General Issues

Certification has been used most widely in international practice in recent years as one of the ways of ensuring the quality of products and services. It simultaneously serves as official confirmation of the competitiveness of the commodity.

Beginning in the 1960s, the concepts, principles, rules and procedures of certification developed and took shape at the international, regional and national levels. In connection with internationalization of trading and industrial relations and creation of a unified economic space under the framework of European communities, efforts were made in developed countries in recent years to unify the terminological, organizational and methodological aspects in connection with documents of the ISO/IEC and the UN EEC.

A special body—the Correspondence Assessment Committee (CASCO)—under the International Standardization Organization (ISO) has been developing the fundamental certification materials. The work of this committee is oriented on providing organizational support to the certification systems being created. Jointly with the International Electrotechnical Committee (IEC) the committee has written an ISO/IEC manual establishing the general terms, the rules for some certification systems, and requirements on testing laboratory accreditation systems.

The United Nations European Economic Commission (EEC) is working on recommendations for concluding certification agreements for use by governments of the European region. These documents are based on the need for finding common principles for regional or bilateral agreements, and their purpose is to prevent establishment of what we call nontariff barriers in international trade.

Several systems for certifying different types of products are presently functioning at the international level. Although they differ in their status, the operating rules are unique to each of these systems. However, all what certification systems have in common is the organizational and methodological approaches at their basis.

With growing integration of countries into a single system of trading and economic relations, they are showing increasing interest in participating in international standardization and certification systems through the development and operation of regional and national systems for assessing correspondence of products and services to the requirements of the standards. The need for a base of technical standards for certification—that is, documents that clearly and unambiguously regulate requirements on the quality of the products to be certified, and pertaining directly to the certification procedure itself—is an important feature of certification.

Basic Concepts, Rules and Procedures of Certification

Certification is methodological and practical activity of a special authorized body aimed at determination, inspection and documentary confirmation of currently existing qualification requirements on personnel, processes, procedures or articles.

According to international requirements, certification may be obligatory or voluntary.

Certification with an obligatory status is conducted when correspondence of an article to the requirements of mandatory standards must be confirmed. Such standards include, in developed foreign countries, technical standards regulating product safety.

Certification on a voluntary basis has the goal of creating relations of trust between the producer and consumer of a product, and ultimately raising its competitiveness.

Depending on the parties participating (legal entities and individuals), certification is classified as:

a manufacturer's statement of correspondence of the product's quality to established norms (self-certification);

certification by a second party;

certification by a third party.

Features of Certifying Pharmaceutical and Medical Products

A system of quality control, certification and standardization of drugs and medical immunobiological preparations, medical articles, food products for therapeutic diets, food additives and cosmetics was developed in the Republic of Kazakhstan in order to permit a unified state policy and strict government control over the

safety and quality of pharmaceutical and medical products entering the republic. This system determines the goals, principles, structure and standard rules of certification.

It should be noted that product certification is one of the means of controlling the safety and quality of such products, based on legal standards and foreseeing observance of standard rules, requirements and norms. This activity is conducted in the republic in accordance with the laws of the Republic of Kazakhstan "On Safeguarding the Health of the People," "On Standardization and Certification," "On Unity of Measurements" and "On Protecting the Rights of Consumers." According to these laws, all imported pharmaceutical and medical products are subject to registration in the republic, and to obligatory certification. Documents regulating the procedure of registration and preclinical and clinical testing of new drugs, medical articles, food products for therapeutic diets and food additives were written and approved for this purpose.

The Administration for Quality Control and Standardization of Drugs and Medical Equipment of the Republic of Kazakhstan Ministry of Health is responsible for regulating, developing and creating the base of standards for quality control and certification of pharmaceutical and medical products. Jointly with the Committee for Standardization, Certification and Metrology under the Republic of Kazakhstan Cabinet of Ministers, the Ministry of Health established the Medstandart State Scientific-Practical Center for Certification and Standardization of Drugs, Medical Articles, and Therapeutic and Preventive Dietary Products (GNPTsS) in order to support development of standards, scientific expert examination of materials, and certification of pharmaceutical and medical products. The center is accredited as the head agency for certification of particular products—drugs and therapeutic cosmetics, medical immunobiological preparations, medical articles and equipment, food products for therapeutic diets, and food additives. Its responsibility includes accreditation of control and analytical laboratories (centers) doing quality control of certified products, and inspecting the activity of accredited testing laboratories.

In accordance with currently effective legislation the Medstandart GNPTsS is determining the principles and procedure of certifying drugs and therapeutic cosmetics, medical immunobiological preparations, medical articles and equipment, food products for therapeutic diets, and food additives, and the procedures of recognizing foreign certificates and examining appeals.

Certification may be applied for by legal entities and individuals: producers, consumers, trade and marketing enterprises, consumer societies etc.

Medical products subject to obligatory certification are imported and sold in the Republic of Kazakhstan in accordance with the "Procedure of Customs Control of Products Subject to Obligatory Certification" approved by the Main Customs Administration of the Ministry of Finance and by the Main State Public Health Physician of the Republic of Kazakhstan.

Products imported from the near and far abroad are certified by recognition of foreign certificates when bilateral or multilateral arrangements exist between the Republic of Kazakhstan and other countries regarding mutual recognition of certification requirements. Measures to certify medical and pharmaceutical products through recognition of the certification documents of CIS countries in accordance with the "Agreement on Principles of Conducting and Mutually Recognizing Certification," signed on 20 October 1993 and effective January 1994, are currently being implemented.

Certification consists of three stages:

preparation of products for certification;

product certification;

control inspections of certified products.

The *preparatory stage* involves familiarizing the client with the rules of certification, selecting the certification scheme, filling out a questionnaire, and filing application documents with the certification agency. These documents include an application, the standard for the product, the questionnaire, and a copy of the payment order submitted in payment of the application fee.

The certification agency evaluates the documents filed by the client, decides if the certification process is to be conducted, and signs a business contract for the work.

Certification. A representative of the certification agency takes samples of the product to be certified in the presence of the client and in accordance with technical standards. The samples are marked, packed, sealed and delivered by the client to the testing laboratory. The certification agency orders the initial tests, and forms a commission of expert auditors to conduct an inspection. A form on which the observations are to be documented is appended to the order for inspection together with a list of the elements of the quality control system or production process to be checked.

The inspectors make the necessary examinations and document their findings on the form indicated above. The inspection results are discussed and documented

by a certificate stating: the goal of the inspection, the revealed inconsistencies, the conclusions, suggestions, and a distribution list.

The certification agency analyzes the testing and inspection results, and draws up an expert opinion. When the results of the inspection are favorable, an order certifying the product submitted by the client is published. In the case of negative test results a notice of denial of a correspondence certificate is sent to the client's address. In addition the agency informs the client of the possibility for continuing the certification process if revealed deficiencies are eliminated within a set period of time.

A blank correspondence certificate is filled out on the basis of the certification order, the certificate is recorded in a log, and it is submitted to the Republic of Kazakhstan State Committee for State Standards for entry in the State Register of the RK GSS [not further identified] together with the registration data, and a licensing agreement is concluded with the client. The term of the certificate is established, and the correspondence certificate is issued.

Control is carried out with the goal of supervising the activity of licensed enterprises; it involves conducting periodic and unscheduled control inspections of samples of the certified product, and control inspections of the quality or production system.

Periodic control inspections are conducted not less than once a quarter. Unscheduled inspections are conducted when the certification agency receives information that the licensee is selling a substandard product. If the results of the inspection are negative, a decision is made to suspend the correspondence certificate, and the conditions for its reinstatement are spelled out in a resolution.

Within 3 days after the period established for meeting the conditions, the certification agency sends a representative to check fulfillment of these conditions. The decision to reinstate the certificate or cancel it is made on the basis of the conclusions and suggestions of the inspector.

The decision to reinstate or cancel is put in writing, and copies of the documents are sent to the client.

Procedure for Recognizing Foreign Certificates. The work of recognizing foreign certificates on products subject to accreditation is carried out if agreements exist on mutual recognition of certification. On the basis of an application for recognition of a foreign certificate, an agreement is signed with the applicant to carry out the certification process. The following are appended to the application: the original foreign certificate or a notarized copy of it, the standard for the product, and other documents established by the rules of the arrangement for certification.

The certification agency checks the authenticity of the certificate and makes a comparative analysis of the requirements of the foreign standard and the requirements of a standard of the Republic of Kazakhstan applicable to the product to be certified.

In the case of recognition of the foreign certificate or of positive inspection results, a correspondence certificate is filled out and issued. When the foreign certificate is untruthful or when inspection results are negative, a decision is made to deny a correspondence certificate, which is then conveyed to the applicant in writing.

Objectives and Problems

The main objective of certification is to ensure safety and quality of drugs, immunobiological preparations, medical equipment and articles, therapeutic dietary products, food additives and hygienic cosmetics, produced in the country and imported.

Because of insufficient development of local pharmaceutical and medical industry, around 95 percent of the demand of the public and of public health institutions of the republic for drugs and medical articles is satisfied by imports, with more than 50 percent of this volume coming from CIS countries. In this case while products coming from the far abroad are first registered with the Ministry of Health, and the corresponding technical standard necessary for quality control is written on them, unfortunately products from CIS countries do not undergo this procedure. There are a number of reasons why purchases of drugs, immunobiological preparations and medical equipment, chiefly from the Russian Federation, Ukraine and Belarus, are handled in this way. First of all these products are well known to specialists, because they are from traditional suppliers; second, these products are much cheaper than Western ones; third, because suppliers have no problems marketing these products in their own countries since the production operations are not functioning at full output, they do not want the added headaches of registering these products in Kazakhstan; finally, deliveries to the republic are made easier by absence of customs barriers with these countries.

However, the number of drugs and medical articles failing to meet the standards has recently been increasing as a result of deliveries of unregistered pharmaceutical and medical products without proper quality control. Consequently introduction of a procedure for certifying pharmaceutical and medical products in accordance with international arrangements of the Republic of Kazakhstan is becoming an urgent matter.

The p ocedure of series-by-series quality control of drugs that has been around for many years is now obsolete, and it is not justified from either the economic or the organizational point of view because the mandatory chemical analyses require significant outlays of reagents, time and labor. The financial outlays on this activity are ultimately added to the product cost. We need to immediately switch to the more progressive, internationally accepted practice of product certification, and conclude bilateral arrangements for certification of products supplied to our country. This approach will make it possible to solve a number of problems, and in particular, it will help to raise the legal guarantees of the safety and quality of drugs and medical articles, it will simplify the control procedure, and it will reduce material and labor outlays.

Training qualified expert auditors, establishing state-of-the-art testing laboratories and centers, and developing the base of laws and standards are serious problems of product certification. Much work has to be done to achieve integration with the international system of certification and standardization.

Ukrainian National Collection of Micro-Organisms

964D0700A Kiev MIKROBIOLOHICHNYY ZHURNAL in English Vol 57 No 6, Nov-Dec 95 pp 3-11

[Article: "Ukrainian national Collection of Micro-Organisms" UDK 579.2:579.8]

[FBIS Transcribed Text] Ukrainian National Collection of Micro-Organisms (UNCM) was established in the D.K. Zabolotny Institute of Microbiology and Virology of National Academy of Sciences of Ukraine—one of the oldest microbiological institutions of Ukraine. The collection maintains and distributes more than 3500 strains of fungi, yeasts, actinomycetes, bacteria and mycoplasmas (both the type cultures and strains isolated from different habitats). UNCM also includes as a branch the culture collection of marine micro-organisms and heterotrophic sliding bacteria of Odessa State University.

In accordance with the department's profile the collection carries on the investigations in the fields of:

—ecology, systematics and population variability of microscopic fungi (more than 900 strains preserved) and their biologically active substances (mycotoxins, melanins, etc.),

—ecology and systematics of yeasts (more than 800 strains), their taxonomic status revision using the results of their life cycle study,

—ecology, systematics and chemotaxonomy of actinomycetes, particularly the nocardio- and coryneforms (500 strains) belonging to genera *Gordona, Rhodococcus, Brevibacterium, Brachybacterium*, etc.,

—systematics, population analysis, the genetic and metabolic peculiarities of methane-oxidizing and methylotrophic bacteria (more than 90 strains),

—ecology and physiology of lactic-acid bacteria, particularly the inhabitants of human and animal gastrointestinal tract (more than 140 strains), creation of probiotic preparations and lactic acid leavens,

—systematics of phytopathogenic bacteria (more than 150 strains), their chemotaxonomy (polyamines, fatty acids), antigenic properties and chemical basis of serotyping,

—systematics and diagnostics of *Pseudomonas, Comamonas* and *Burkholderia* genera (more than 350 strains), chemical structure and biological activity of antibiotics produced by these micro-organisms,

—ecology, systematics and chemotaxonomy of Gram-positive catalasepositive aerobic cocci (more than 250 strains),

—biology of aerobic spore-forming bacilli (more than 250 strains), their enzymatic and antibiotic activity, creation of probiotic preparations,

—ecology, physiology and biotechnology of free-living and symbiotrophic nitrogen-fixing bacteria of genera *Azotobacter, Rhizobium*, and *Bradyrhizobium* (more than 200 strains),

—systematics of *Mycoplasmas* (50 strains) and molecular mechanisms of their biological activity including the pathogenicity to plants and animals,

—biology, ecology and systematics of marine micro-organisms and heterotrophic sliding bacteria (45 strains).

Collection includes 274 type strains of micro-organisms and more than 300 strains of biotechnological importance.

Here we present the list of microbial strains maintained in the Ukrainian National Collection of Micro-Organisms.

The designation "o" indicates that the strains of that species are maintained in Odessa branch of UNCM.

The designation "*" indicates that the type strain of the species is maintained in UNCM.

List of Strains of Micro-Organisms Maintained in the Ukrainian National Collection of Micro-Organisms

Genus	Species	No. of strains
Fungi		
Acremonium	murorum	4
Acremonium	sp.	1
Aspergillus	alliaceus	6
Aspergillus	amsterdami	3
Aspergillus	amylovorus	6
Aspergillus	awamori	3
Aspergillus	candidus	14
Aspergillus	carbonarius	3
Aspergillus	carneus	4
Aspergillus	clavatus	27
Aspergillus	fischeri	13
Aspergillus	flavus	11
Aspergillus	foetidus	3
Aspergillus	fumigatus	25
Aspergillus	leucocarpus	1
Aspergillus	niger	10
Aspergillus	ochraceus	3
Aspergillus	oryzae	12
Aspergillus	pallidus	13
Aspergillus	parasiticus	7
Aspergillus	parvulus	8
Aspergillus	ruber	6
Aspergillus	sclerotiorum	14
Aspergillus	terreus	12
Aspergillus	terreus var. aureus	3
Aspergillus	ustus	36
Aspergillus	versicolor	6
Aspergillus	versicolor	21
Aspergillus	wentii	10
Aureobasidium	pullulans	11
Botrytis	allii	2
Botrytis	cinerea	3
Chaetomium	sp.	1

Genus	Species	No. of strains
Cladosporium	cladosporioides	17
Cladosporium	herbarum	12
Cladosporium	sphaerospermum	10
Corynascus	sepedonium	5
Curvularia	inaequalis	6
Dactylaria	gallopava	1
Dendrodochium	toruosum	8
Embellisia	alli	1
Fusarium	sp.	1
Fusarium	avenaceum	30
Fusarium	avenaceum var.herbarum	2
Fusarium	buharicum	2
Fusarium	culmorum	22
Fusarium	gibbosum	42
Fusarium	gibbosum var. acuminatum	9
Fusarium	gibbosum var. bullatum	10
Fusarium	graminearum	24
Fusarium	heterosporum	5
Fusarium	javanicum	15
Fusarium	javanicum var. radicicola	6
Fusarium	lateritium	11
Fusarium	macrosporum	5
Fusarium	merismoides	3
Fusarium	moniliforme	11
Fusarium	moniliforme var. lactis	32
Fusarium	moniliforme var. subglutinans	11
Fusarium	oxysporum	11
Fusarium	oxysporum var.orthoceras	101
Fusarium	roseum	3
Fusarium	sambucinum	31
Fusarium	sambucinum var. minus	16
Fusarium	sambucinum var. coccicolum	2
Fusarium	sambucinum var. subhaustum	4
Fusarium	semitectum	13
Fusarium	solani	23
Fusarium	solani var. argillaceum	20

Genus	Species	No. of strains
Fusarium	sporotrichiella	21
Fusarium	sporotrichiella var. anthophilum	2
Fusarium	sporotrichiella var. poae	17
Fusarium	sporotrichiella var. tricinctum	1
Fusarium	trichothecioides	1
Hapsidospora	milkii	1
Humicola	fuscoatra	2
Humicola	grisea	5
Melanocarpus	albomyces	4
Malbranchea	pulchella sulfurea	1
Mitrogamella	atrophila	1
Myrothecium	roridum	3
Myrothecium	verrucaria	3
Nigrospora	oryzae	2
Oidiodendron	cerealis	4
Papulaspora	thermophila	3
Paecilomyces	lilacinus	4
Penicillium	canescens	6
Penicillium	citreo-viride	1
Penicillium	citrinum	1
Penicillium	expansum	1
Penicillium	felitanum	1
Penicillium	restrictum	1
Penicillium	verruculosum	1
Penicillium	viride	1
Rhizomucor	pusillus	6
Rhizomucor	tauricus	1
Rhizopus	oryzae	1
Stachybotrys	alternans	3
Stachybotrys	chartarum	5
Thermoascus	aurantiacus	6
Thermoascus	crustaceus	2
Trichocladium	asperum	4
Trichoderma	sp.	1
Ulocladium	consortiale	8
Yeasts		

Genus	Species	No. of strains
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	6*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	4
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	4*
Candida	[illegible]	90*
Candida	[illegible]	17*
Candida	[illegible]	1
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	20*
Candida	[illegible]	1*
Candida	[illegible]	1*
Candida	[illegible]	1*

Genus	Species	No. of strains
Candida	rugosa	1*
Candida	sake	1*
Candida	savonica	1*
Candida	schatavi	1*
Candida	silvae	1*
Candida	silvatica	1*
Candida	sorbophila	1*
Candida	sorboxylosa	1*
Candida	tenuis	1*
Candida	tenuis	1*
Candida	tropicalis	40
Candida	utilis	6*
Candida	valida	25*
Candida	vanua	1*
Candida	vini	10*
Candida	xylanoides	1*
Cryptococcus	albidus var albidus	45
Cryptococcus	laurentii	40
Cryptococcus	terreus	1
Cryptococcus	unigutulatus	2
Debaryomyces	castellii	1*
Debaryomyces	hansenii var hansenii	20*
Debaryomyces	polymorphus	10*
Debaryomyces	vanrij var vanrij	1
Hanseniaspora	uvarum	1
Issatchenkia	occidentalis	1*
Issatchenkia	orientalis	1*
Kloeckera	apiculata	10
Kloeckera	spp	1
Kluyveromyces	marxianus var marxianus	10*
Kluyveromyces	marxianus var bulgaricus	2*
Kluyveromyces	marxianus var drosophilarum	1*
Kluyveromyces	marxianus var lactis	5
Kluyveromyces	thermotolerans	1*
Kluyveromyces	wickerhamii	1*

Genus	Species	No. of strains
Metschnikowia	[illegible]	1*
Metschnikowia	[illegible]	30
Pachysolen	[illegible]	1*
Pichia	[illegible]	40
Pichia	[illegible]	1*
Pichia	[illegible]	1*
Pichia	[illegible]	1*
Pichia	[illegible]	15*
Pichia	[illegible]	1*
Pichia	[illegible]	1
Rhodosporidium	[illegible]	3*
Rhodosporidium	[illegible]	2*
Rhodotorula	[illegible]	5
Rhodotorula	[illegible]	50
Rhodotorula	[illegible]	5
Rhodotorula	[illegible]	50
Saccharomyces	[illegible]	50
Saccharomyces	[illegible]	5
Saccharomyces	[illegible]	10
Schizosaccharomyces	[illegible]	1*
Schizosaccharomyces	[illegible]	1*
Schwanniomyces	[illegible]	9*
Schwanniomyces	[illegible]	1*
Sporobolomyces	[illegible]	4
Trichosporon	[illegible]	10
Trichosporon	[illegible]	4
Williopsis	[illegible]	2
Williopsis	[illegible]	15
Williopsis	[illegible]	20
Yamadazyma	[illegible]	50*
Yamadazyma	[illegible]	1*
Yamadazyma	[illegible]	1*
Yamadazyma	[illegible]	1*
Yarrowia	[illegible]	5
Eubacteria		
[illegible]	("A. [illegible]")	1

Genus	Species	No. of strains
Aeromonas sp.	("A. dechromatica")	1
Agrobacterium	tumefaciens	10*
Alteromonas	atlantica	1*
Alteromonas	carrageenovora	1*
Alteromonas	haloplanktis	1*
Alteromonas	macleodii	1*
Alteromonas	nigrifaciens	1*
Alteromonas	sp.	3
Alteromonas	tetraodonis	1*
Archangium	gephyra*	1
Azotobacter	chroococcum	16
Azotobacter	vinelandii	1
Bacillus	badius	1*
Bacillus	brevis	2*
Bacillus	cereus	21*
Bacillus	circulans	4
Bacillus	coagulans	4*
Bacillus	firmus	1
Bacillus	laterosporus	1*
Bacillus	licheniformis	31*
Bacillus	longisporus	1*
Bacillus	macerans	2
Bacillus	megaterium	23
Bacillus	sp. ("B. mucilaginosus")	1
Bacillus	mycoides	3
Bacillus	pasteurii	1*
Bacillus	polymyxa	9*
Bacillus	pumilus	17*
Bacillus	sphaericus	1*
Bacillus	stearothermophilus	1
Bacillus	subtilis	131*
Bacillus	thuringiensis	2*
Bifidobacterium	bifidum	1
Bifidobacterium	longum	1*
Bifidobacterium	pullorum	1*
Bradyrhizobium	japonicum	20

Genus	Species	No. of strains
[illegible]	[illegible]	14
[illegible]	[illegible]	2*
[illegible]	[illegible]	2*
[illegible]	[illegible]	10*
[illegible]	[illegible]	1*
[illegible]	[illegible]	2*
[illegible]	[illegible]	1*
[illegible]	[illegible]	1*
[illegible]	[illegible]	17*
[illegible]	[illegible]	7*
[illegible]	[illegible]	1*
[illegible]	[illegible]	9*
[illegible]	[illegible]	1*
[illegible]	[illegible]	1
[illegible]	[illegible]	1
[illegible]	[illegible]	6
[illegible]	[illegible]	7
[illegible]	[illegible]	2*
[illegible]	[illegible]	1*
[illegible]	[illegible]	1
[illegible]	[illegible]	1*
[illegible]	[illegible]	1*
[illegible]	[illegible]	1
[illegible]	[illegible]	1*
[illegible]	[illegible]	1*
[illegible]	[illegible]	9
[illegible]	[illegible]	1*
[illegible]	[illegible]	1
[illegible]	[illegible]	9*
[illegible]	[illegible]	8
[illegible]	[illegible]	10*
[illegible]	[illegible]	2*
[illegible]	[illegible]	1*
[illegible]	[illegible]	9*
[illegible]	[illegible]	1*
[illegible]	[illegible]	11

Genus	Species	No. of strains
Erwinia	chrysanthemi	2*
Erwinia	herbicola	3*
Erwinia	quercina	1
Erwinia	rhapontici	2
"Flavobacterium	arborescens"*	1
"Flavobacterium	aurantiacum"*	1
Flavobacterium	devorans*	1*
Flavobacterium	ferrugineum*	1
Flavobacterium	marinotypicum*	1*
Flavobacterium	okeanokoites*	1*
Flavobacterium	resinovorum*	1*
Flavobacterium	vulcanense*	1*
"Flexibacter	elegans"*	1*
"Flexibacter	filiformis"*	1*
Flexibacter	flexilis	1*
Flexibacter	flexilis var. algavorum*	1
Flexibacter	sancti*	2*
Flexibacter	tractuosus*	1*
Lactobacillus	acidophilus	17
Lactobacillus	agilis	1
Lactobacillus	animalis	8
Lactobacillus	brevis	1
Lactobacillus	buchneri	6*
Lactobacillus	casei subsp. casei	3
Lactobacillus	casei subsp. tolerans	1
Lactobacillus	delbrueckii subsp. bulgaricus	1
Lactobacillus	delbrueckiisubsp.delbrueckii	5*
Lactobacillus	fermentum	9
Lactobacillus	plantarum	12
Lactobacillus	reuteri	1
Lactobacillus	ruminis	2
Lactobacillus	salivarius	10
Lactobacillus	sp.	2
Lactobacillus	viridescens	1*
Lactobacillus	yamanashiensis	1*
Lactococcus	lactis subsp. cremoris	1

Genus	Species	No. of strains
Lactococcus	lactis subsp. lactis	1*
Leuconostoc	mesenteroides subsp. dextranicum	1
Leuconostoc	mesenteroides subsp. mesenteroides	1*
Lysobacter	antibioticus*	1*
Lysobacter	gummosus*	1*
Methylobacter	luteus	8*
Methylobacter	sp.	5
"Methylobacter	ukrainicus"	4*
Methylobacter	whittenburyi	1*
Methylobacterium	extorquens	10
Methylobacterium	fujisawaense	2*
Methylobacterium	mesophilicum	7*
Methylobacterium	organophilum	3
Methylobacterium	sp.	10
Methylococcus	capsulatus	3
"Methylococcus	gracilis"	2*
Methylocystis	echinoides	1
Methylocystis	sp.	2
Methylocystis	parvus	4*
Methylomonas	methanica	2*
"Methylomonas	rubra"	7*
Methylomonas	sp.	2
Methylosinus	sp.	2
Methylosinus	sporium	4*
Methylosinus	trichosporium	6*
Microcilla	marina*	2
Myxococcus	coralloides*	1*
Myxococcus	fulfur*	2
Myxococcus	virescens*	1
Myxococcus	xanthus*	2*
Pediococcus	pentosaceus	2
Planococcus	citreus	1*
"Polyangium	cellulosum"*	1
Polyangium	sp.*	1
Pseudomonas	aeruginosa	41*
Pseudomonas	alcaligenes	3*

Genus	Species	No. of strains
Pseudomonas	auratiaca	25*
Pseudomonas	aurofaciens	8*
Pseudomonas	chlororaphis	2*
Pseudomonas	fluorescens	66*
Pseudomonas	fragi	15*
Pseudomonas	glathei	1*
Pseudomonas	lundensis	1*
Pseudomonas	mendocina	5*
Pseudomonas	pseudoalcaligenes	22*
Pseudomonas	putida	31*
Pseudomonas	saccharophila	1*
Pseudomonas	stutzeri	4*
Pseudomonas	syringae	1*
Pseudomonas	syringae pv. atrofaciens	18*
Pseudomonas	syringae pv. coronofaciens	5
Pseudomonas	syringae pv. glycinea	1
Pseudomonas	syringae pv. lachrymans	18
Pseudomonas	syringae pv. maculicola	1
Pseudomonas	syringae pv. [illegible]	2
Pseudomonas	syringae pv. phaseolicola	6*
Pseudomonas	syringae pv. pisi	1
Pseudomonas	syringae pv. syringae	7
Pseudomonas	tartrolens	1*
Pseudomonas	viridiflava	1
Rhizobium	galega	12
Rhizobium	leguminosarum	21
Rhizobium	meliloti	6
Shewanella	putrefaciens	1*
Sphingomonas	paucimobilis	1*
Streptococcus	bovis	2*
Streptococcus	equinus	1
Streptococcus	salivarius subsp. thermophilus	4
Staphylococcus	aureus subsp. aureus	22
Staphylococcus	capitis subsp. capitis	1*
Staphylococcus	chromogenes	1*
Staphylococcus	cohnii subsp. cohnii	1*

Genus	Species	No. of strains
Staphylococcus	cpidermis	1*
Staphylococcus	haemolyticus	1*
Staphylococcus	intermedius	1*
Staphylococcus	lentus	1*
Staphylococcus	chromogenes	1*
Staphylococcus	saprophyticus	1*
Staphylococcus	sciuri	1*
Staphylococcus	simulans	1*
Staphylococcus	xylosus	1*
Staphylococcus	sp.	100
Stenotrophomonas	maltophilia	54*
Xanthomonas	campestris	1
Xanthomonas	campestris pv. campestris	9
Xanthomonas	campestris pv. carotae	1
Xanthomonas	campestris pv. cucurbitae	2
Xanthomonas	campestris pv. glycines	1
Xanthomonas	campestris pv. holcicola	2
Xanthomonas	campestris pv. hyacinthi	1
Xanthomonas	campestris pv. malvacearum	5
Xanthomonas	campestris pv. oryzae	1
Xanthomonas	campestris pv. phaseoli	5
Xanthomonas	campestris pv. translucens	1*
Xanthomonas	campestris pv. vesicatoria	6
Mollicutes		
Acholeplasma	axanthum	1*
Acholeplasma	granularum	1*
Acholeplasma	hippicon	1*
Acholeplasma	laidlawii	38
Acholeplasma	modicum	1*
Acholeplasma	morum	1*
Acholeplasma	oculi	1*
Mycoplasma	capricolum	1*
Mycoplasma	fermentans	1*
Mycoplasma	hominis	1*
Mycoplasma	mycoides var. capri	1*

Genus	Species	No. of strains
Mycoplasma	pneumoniae	1*
Mycoplasma	salivarium	1*
Actinomycetes		
Arthrobacter	agilis	1*
Arthrobacter	citreus	1*
Arthrobacter	globiformis	2*
Arthrobacter	nicotianae	1*
Arthrobacter	oxydans	1*
Arthrobacter	protophormiae	2*
Arthrobacter	sulfureus	2*
Arthrobacter	ureafaciens	1*
Aureobacterium	barkeri	1*
Aureobacterium	liquefaciens	1*
Aureobacterium	saperdae	1*
Aureobacterium	testaceum	1*
Brachybacterium	sp.	24
Brachybacterium	faecium	1*
Brachybacterium	zesterrakovii	3*
Brevibacterium	iodinum	1
Brevibacterium	linens	4
Cellulomonas	cellasea	1*
Cellulomonas	cellulans	2
Cellulomonas	flavigena	1*
Cellulomonas	turbata	1*
Cellulomonas	uda	1*
Clavibacter	michiganensis	2*
	subsp. insidiosus	
Clavibacter	michiganensis	4*
	subsp.michiganensis	
Clavibacter	michiganensis	2
	subsp. sepedonicus	
Corynebacterium	ammoniagenes	2*
Corynebacterium	glutamicum	3
Corynebacterium	sp.	2
Corynebacterium	variabilis	2*
Corynebacterium	vitarumen	1*

Genus	Species	No. of strains
Corynebacterium	[illegible]	1*
Corynebacterium	[illegible]	1*
Corynebacterium	[illegible]	1*
Corynebacterium	[illegible]	1*
Dermacoccus	[illegible]	1*
Dietzia	[illegible]	30*
Gordona	[illegible]	1*
Gordona	[illegible]	63*
Gordona	[illegible]	14*
Kocuria	[illegible]	3*
Kocuria	[illegible]	23*
Kocuria	[illegible]	10sup>*
Kytococcus	[illegible]	1*
Microbacterium	[illegible]	1*
Microbacterium	[illegible]	1*
Microbacterium	[illegible]	1*
Micrococcus	[illegible]	25*
Micrococcus	[illegible]	1*
Micrococcus	[illegible]	80
Mycobacterium	[illegible]	1*
Nocardia	[illegible]	1*
Nocardia	[illegible]	1*
Nocardia	[illegible]	1*
Nocardioides	[illegible]	4*
Nocardioides	[illegible]	1*
Nocardioides	[illegible]	1*
Nocardioides	[illegible]	1*
Promicromonospora	[illegible]	1*
Rhodococcus	[illegible]	1*
Rhodococcus	[illegible]	1*
Rhodococcus	[illegible]	83*
Rhodococcus	[illegible]	1
Rhodococcus	[illegible]	39*
Rhodococcus	[illegible]	1*
Rhodococcus	[illegible]	8*
Rhodococcus	[illegible]	23*

Genus	Species	No. of strains
Rhodococcus	sp. (R. ruberpertinctus)	1
Rhodococcus	sp. ("R. aquosus")	3*
Rhodococcus	sp. ("R. flavus")	3
Rhodococcus	sp. (R. longus")	1
Rhodococcus	sp. ("R. opacus")	7
Saccharopolispora	rectivirgula	1*
Streptomyces	achromogenes	1*
Streptomyces	afganiensis	2
Streptomyces	albidoflavus	1*
Streptomyces	albovinaceus	1
Streptomyces	albus	6*
Streptomyces	ambofaciens	1
Streptomyces	antibioticus	1
Streptomyces	atroolivaceus	1
Streptomyces	aureofaciens	1*
Streptomyces	bikiniensis	1
Streptomyces	californicus	1
Streptomyces	chrysomallus	1
Streptomyces	flaveolus	1
Streptomyces	flavochromogenes	2*
Streptomyces	flavoviridis	1*
Streptomyces	fradiae	2*
Streptomyces	fragilis	1*
Streptomyces	galilaeus	1
Streptomyces	globisporus	5
Streptomyces	globosus	1
Streptomyces	griseolus	1*
Streptomyces	griseoviridis	1
Streptomyces	griseus	5
Streptomyces	halstedii	3
Streptomyces	helvaticus	2
Streptomyces	intermedius	1
Streptomyces	lavendulae	2*
Streptomyces	lincolnensis	2
Streptomyces	longisporoflavus	2
Streptomyces	mashuensis	2

Genus	Species	No. of strains
Streptomyces	odorifer	2
Streptomyces	olivaceoviridis	1
Streptomyces	olivaceus	6*
Streptomyces	olivoreticuli	1
Streptomyces	platiscleroticus	3
Streptomyces	pseudogriseolus	1
Streptomyces	roseiscleroticus	1
Streptomyces	rosiomycinicus	2
Streptomyces	sindenensis	1
Streptomyces	sp.	55
Streptomyces	toxytricini	1
Streptomyces	violaceoruber	5
Streptomyces	violaceus	1*
Terrabacter	tumescens	1*

Pseudomonas cichorii: Potentially Dangerous Disease Agent for Agricultural Crops in Ukraine

964D0701A Kiev MIKROBIOLOHICHNYY ZHURNAL in Russian Vol 57 No 6, Nov-Dec 95 pp 12-19

[Annotation and Article by V. A. Muras, L. D. Varbanets, N. V. Zhitkevich, R. I. Gvozdyak, Z. P. Vasyurenko, N. V. Moskalenko, Institute of Microbiology and Virology, National Academy of Sciences of Ukraine, Kiev; Kiev Scientific Research Institute of Epidemiology and Infectious Diseases; (manuscrip received 12 Jul 94) UDC 579.841.11.222]

[FBIS Translated Text]

Annotation

The typical strain *P. cichorii* 9048 distinguishes itself from *Pseudomonas* phytopathogens in a number of phenotypical properties. The species is a serologically distinct group of bacteria which has no or few antigens in common with other bacteria species. The fatty acid content of lipid A contains more than eight acids. It is characterized by a low content of unsaturated fatty acids, represented only by one hexadecenic acid and the absence of cyclopropanic acids. The dominant fatty acids are tetradecanoic and 3-oxytetradecanoic acids. The fatty acid spectra also reveal the presence of dodecanoic, hexadecanoic, 3-oxyhexadecanoic and 3-oxyoctadecanoic acids.

At present *P. cichorii* is not widespread as an agent of bacteriosis in agricultural crops in Ukraine. *P. cichorii* was isolated from diseased plants. Considering that the species is highly aggressive in artificial infection for a number of agricultural crops, especially for tomatoes and peppers, one can assume that in the future in our country peppers and tomatoes will be among the crops infected in the natural conditions of *P. cichorii*.

Pseudomonas cichorii was first isolated in 1925 from chicory with indications of rot on the young leaves, as well as from dark-brown necrotic spots.[22] According to the data of Thornberry,[23] Okabe obtained positive results in artificial infection of a number of plants with this agent. In subsequent years the bacteria was described as an agent of leaf spot in lettuce in California,[16] leaf rot of peppers in Cuba,[20] bacteriosis of endive in the Republic of Burundi,[13] tomatoes in New Zealand,[14] chrysanthemums in the Netherlands,[17] and several other plants.

With the exception of brief reports by Khodos[10] and Pendus et al.,[9] who detected *P. cichorii* in carrots and ginseng respectively, there is no literature data on the appearance of this agent in the territory of the former soviet Union.

P. cichorii, according to Bergey's guidebook,[11] is in a group with homologous RNA and DNA that includes *P. syringae* (and its pathovars) and *P. viridiflava*. In terms of RNA homology, *P. cichorii* is grouped with conditionally pathogenic species (*P. aeruginosa, P. fluorescens*) and seven species of saprophytes. It falls into other groups by DNA homology. *P. cichorii* of all

the aforementioned representatives of phytopathogenic *Pseudomonas is closest to the conditional pathogens and saprophytes, to P. aeruginosa.*

All of the aforementioned species of bacteria are classified in one section due to a number of properties. However, in this group *P. cichorii* is distinct: it has fluorescing pigment, cytochrome-c-oxidase, arginindehydrolase is absent, and it does not form poly-β-hydroxybutyrate as a reserve material. In contrast to *P. syringae* and *P. viridiflava, P. cichorii* is an oxidase-positive species and does not have ribonucleases. This species differs from *P. viridiflava* also in its inability to use D(- -tartrates, sorbitol, and several other organic sources of carbon.

This paper presents the results of the study of several phenotypical, chemotaxonomic and antigenic properties of a typical strain of *P. cichorii.*

Material and Methods. The object of study was the typical strain *P. cichorii* IMV 9048 (ATCC 10857, ICMP 5707, NCPPB 943) obtained from ICMP. The morphological and cultural properties were studied in cultivation of the strain on potato agar, beef extract agar (BEA), beef extract bouillon (BEB), and colored media.[1]

In the study of the serological properties the Gruber-Vidalia agglutination reaction was used[2] as well as double diffusion in agar using Ouchterlony's method.[3] In these reactions OH-and O-antisera were used. The latter was obtained by immunizing rabbits with bacterial cells heated to 100°C for 2.5 hours. The antigens were a 24-hour live culture (OH-antigen) and antigens obtained using Grasset's method.[3] The Grasset antigens were thermolabile (unheated) and thermostable (heated to 100°C for 2.5 hours).

The composition of the lipid component of the lipopolysaccharides of *P. cichorii* 9048 was determined by methylation of fatty acids with 3 percent solution of hydrochloric acid in methanol at 100°C for four hours. The methyl ethers were analyzed in a Tsvet-110 gas chromatograph in a flame-ionization detector and column filled with 1 percent SE-30 in a choromosorb W(AW-DMCS) with a granule size of 60-100 mesh. The temperature was programmed from 120 to 225°C with a rate of heating of 3°C/min. Identification of the components was done by comparison of their retention time with the retention time of standards.[5] Hydrogenation and bromation was used to determine the unsaturated fatty acids.[6] Hydroxy acids were determined with trifluoracetylation.[6]

The virulent properties of *P. cichorii* were verified under greenhouse and field conditions with peppers, tomatoes, tobacco, potatoes, feed beans, beans, beets, sunflowers, pumpkins, watermelons, ginseng and Ka'ankhoye.[1]

Results and Discussion. The results of microscopic studies indicate that the morphology of cells and colonies of *P. cichorii* 9048 is typical for phytopathogenic *Pseudomonas* bacteria. It is comprised of slightly curved rods with rounded ends, and is mobile, gram-negative, and aerobic. Colonies on potato agar were grayish-white, shiny, round, elevated with a slightly wavy edge, and transparent (Figure 1—not reproduced). On BEA the colonies were similar but somewhat more delicate and transparent. The bacteria grow well in BEB where they form fluorescing pigment. This pigment is formed in growth on potato agar and BEA. The main cultural-biochemical properties of *P. cichorii* are presented in Table 1.

Table 1. Cultural-Biochemical Properties of P. cichorii strain 9048.

Property	Presence or absence
Use of food sources by oxidation	
Glucose, galactose, saccharose, xylose, rhamnose, mannitol	+
Lactose, maltose, dulcitol, sorbitol, salicin, arginine	
Litmus serum, gelatin	
Reduction of nitrates	+
Indole, hydrogen sulfide, levan	

Property	Presence or absence
Oxidase, lecithinase	+
Demand for growth factors	-

In the search for producers of phytohormones among phytopathogenic *Pseudomonas* bacteria it was found that *P. cichorii* 9048 was the only strong producer of indoleacetic acid. Strains of the pathovars of *P. syringae*, *P. viridiflava*, *P. fluorescens*, *P. aeruginosa*, *P. putida* and *P. chlororaphis* did not form or formed very little indoleacetic acid.

Serological studies are significant in the systematic classification of bacteria for identification . Few papers are devoted to the antigen composition of *P. cichorii*. Among them, first place is held by the research of Gouk et al.,[10] who studied the serological link between *P. cichorii* and 48 species of *Pseudomonas*, *Corynebacterium*, *Erwinia*, and *Xanthomonas* bacteria.

The results of our research overall agree with the results of these researchers. Our data indicate the absence of an antigenic similarity between these bacteria because the serum of live and heated cultures (titers of 25600 and 6400 respectively) reacted to almost none of the tested 66 strains representing various species of bacteria (*Pseudomonas gladioli* pv. *alliicola*, *P. solanacearum*, *P. syringae* pv. *atrofaciens*, pv. *coronafaciens*, pv. *corrugata*, pv. *glycinea*, pv. *holci*, pv. *lachrymans*, pv. *mori*, pv. *persicae*, pv. *phaseolicola*, pv. *pisi*, pv. *tabaci*, pv. *tomato*, pv. *syringae*, *P. viridiflava*, *P. fluorescens*, *P. marginalis* pv. *marginalis*, pv.*pastinacae*, *P. aeruginosa*, *P. cepacia*, *Xanthomonas campestris* pv. *campestris*, pv. *phaseoli*, pv. *vesicatoria*, *Clavibacter michiganense* ssp. *michiganense*, *Erwinia carotovora* ssp. *carotovora*, *Erwinia herbicola*). The antiserum of *P. cichorii* interacted with strains of the species *P. tabaci*, *P. viridiflava* and *P. solanacearum* only in a very low titer (200, 400) in the Gruber-Vidalia reaction. The reaction probably occurred due to common nonspecific minor agglutinogens of unknown origin.

No common antigens were detected in the interaction of *P. cichorii* with polyvalent antiserum to the heterogeneous species *P. syringae*, and the antiserum to *P. (Burkholderia) solanacearum*. In double diffusion reactions in agar using thermostable and thermolabile antigens no common lines of precipitation were observed.

Thus, *P. cichorii* is an isolated serologically distinct group of bacteria which has no antigens in common with other species of bacteria.

The absence of a serological interrelation between *P. cichorii* and *P. solanacearum* was somewhat unexpected due to our earlier studies[2] on the structure of O-PS [expansion not given] typical strains of *P. cichorii* and *P. solanacearum*. It was found that O-PS cultures are characterized by a similar structure represented by pentasaccharide repeating chains including three rhamnose residues, one residue of N-acetyl-β-glucosamine and one residue of β-xylose in the form of a lateral chain. One can assume that not all similar O-PS structures are responsible for serological affinity.

Among hemotaxonomic phenotypical indicators researchers accord special importance to the content of cellular fatty acids of bacteria. The fatty acid content of cells is particularly used to solve debates on the classification and identification of new and heterogenic taxons.[4,5] For the strain of *P. cichorii* 9048 that we studied lipid A is characterized by a low content of unsaturated fatty acids, represented by only one hexadecenic acid (C 16:1) and the absence of cyclopropanic acids (Table 2). The dominant fatty acids in the studied strain of *P. cichorii* are tetradecanoic (C 14:0) and 3-oxytetradecanoic acid (C 14:0 3-OH).

Table 2. Content of Fatty Acids of Lipid A of P. cichorii 9048 (ratio given in percent by area of peaks of gas-liquid chromatography).

Fatty acid	Amount, %
Dodecanoic (C 12:0)	0.4
Tetradecanoic (C 14:0)	24.7
3-oxytetradecanoic (C 14:0 3-OH)	39.9
Hexadecenic (C 16:1)	2.9
Hexadecanoic (C 16:0)	2.7
3-oxyhexadecanoic (C 16:0 3-OH)	22.8
Octadecanoic (C 18:0)	Trace
3-oxyoctadecanoic (C 18:0 3-OH)	3.0
Unidentified acids	10.2

P. cichorii contains 3-oxytetradecanoic and 3-oxyhexadecanic acids in lipid A which makes it similar to other representatives of section 2.[7,23] However, in contrast to the latter, the lipopolysaccharides of *P. cichorii* (as in *P. solanacearum*) contain 3-oxyoctadecanoic acid.

Our results on the study of the fatty acid composition of lipid A differ from data presented by Stead[21] who studied fatty acids in hydrolyzates of *P. cichorii* cells. The main differences are that Stead did not detect 3-oxytetra-hexa- and octadecanoic acids in the cellular lipids of *P. cichorii*, but did detect 2-oxy-and 3-oxydodecanic acids. The reason for these differences has not yet been explained.

Analysis of our results showed that the species *P. cichorii* and *P. solanacearum* which occupy different positions in the classification system, in the absence of serological similarity have an identical O-PS structure and a similar fatty acid composition of lipid A.[3] One can assume that common determinants are screened in them. It has not been ruled out that the secondary structure of the lipopolysaccharides may affect the serological specificity. In the literature there is data that the O-PS structures of *P. cepacia* and *P. aeruginosa* are identical (serotypes and serogroups were determined) and they are also in different groups in the system.[9] The fatty acid composition of lipid A in *P. cichorii* differs from such other phytopathogenic species by the presence of 3-oxyoctadecanic acid, which has not been detected to date in the composition of lipid A in other species of *Pseudomonas* bacteria except *P. solanacearum*.

An important property of a bacterial agent is the manifestation of its virulent properties. Experiments that we conducted over the course of a number of years on artificial infection of many agricultural plants showed that *P. cichorii* is very aggressive toward a number of economically important crops. In an experiment in a greenhouse in artificial infection of the leaves of pepper plants, gray-olive and brown spots were formed, sometimes with a darker edge. The leaf may curl up and droop. The infection of leaves in the field gave a weak picture of the manifestation of the disease because the latter is manifested better in the fruit. Peduncles of flowers manifested dry gray spots 0.3-0.5 cm in diameter. Fruit exhibited olive-brown spots which were distinct from healthy tissue, which then became black, frequently taking an elongated shape. In the field one could observe a brilliant picture of infection: bright-black spots with a light aureole on the rose-red background of the fruit. Thereafter the fruit usually rotted, its contents softened, it acquired an olive color and the skin drooped but did not fall off (Figures 2a and 2b—not reproduced).

On tomatoes in a greenhouse 2-5 days after inoculation of 2-4 week plants the leaves and branches wilted (Figure 3—not reproduced). If the plant was weakened, the entire plant might die. In field conditions the disease is manifested only in the fruit, which forms dark spots. The fruit frequently rots.

The leaves of tobacco plants alone exhibited a supersensitive reaction characteristic of phytopathogenic *Pseudomonas* bacteria. Beige-brown necrotic spots formed where the bacterial suspension was introduced.

In bean plants in artificial infection with *P. cichorii* 9048 only the beans formed small (2-3 mm) oily brown-black spots.

In feed beans in infection of the stem one could observe light-brown bands up to 2 cm long and on the beans, small black dry spots. In beets in the field at the punctures on the stem black bands-cracks up to 3 cm in length formed.

In the infection of potatoes, sunflowers, watermelons, pumpkins, ginseng and Kalanchoye with *P. cichorii* culture negative results were obtained.

Thus, *P. cichorii* is highly virulent for some Solanaceae (peppers, tomatoes), and slightly virulent for beans, feed beans, and beets.

Consequently, a feature of *P. cichorii* (typical strain) is the significant isolation of a number of phenotypical properties (biochemical, serological) from other such species of *Pseudomonas* phytopathogens. An exception is *P. solanacearum* (typical strain) which is characterized by an identical O-PS structure and a very similar fatty acid content of lipid A. *P. cichorii* is highly virulent for a number of important agricultural crops. Thus, it can be assumed that in the near future pepper and tomato plants, which are highly sensitive to this agent, will be among the crops infected under the natural conditions with *P. cichorii*.

References

1. K. I. Beltyukova, M. S. Matyshevskaya, M. D. Kulikovskaya, S. S. Sidorenko, *Metody issledovaniya vozbuditeley bakterialnykh bolezney rasteniy* [Methods of Studying Agents of Bacterial Diseases of Plants] Kiev: Nauk. dumka, 1968 316 pp.

2. L. D. Varbanets, N. A. Kocharova, Yu. A. Knirel et al., "Lipopolysaccharides of *Pseudomonas solanacearum* MIKROBIOL. ZHUR. Vol 52 No 4, 1990 pp 27-33.

3. L. D. Varbanets, V. A. Muras, R. I. Gvozdyak et al., *Lipopolysaccharides of Pseudomonas solanacearum* and

Pseudomonas cichorii" MIKROBIOL. ZHURN. Vol 54 No 2, 1992 pp 26-31.

4. Z. P. Vasyurenko, Ye. N. Chernyavskaya, L. V. Openko, *Features of the Fatty Acid Composition of Lipids in Providencia alcalifaciens* and *Providencia stuarti*" MIKROBIOLOGIYA Vol 51 No 1, 1982 pp 54-59.

5. Z. P. Vasyurenko, A. P. Prolov, V. V. Smirnov, N. M. Ruban. *Zhirnokislotnyye profili bakterty, patogennykh dlya cheloveka i zhivotnykh* [Fatty Acid Profiles of Bacteria Pathogenic to Man and Animals] Kiev: Nauk. dumka, 1992 264 pp.

6. O. Ye. Zherebilo, N. M. Vishtalyuk, "Fatty Acids of Common Lipids of Several Representatives of the Genus *Erwinia* and other Enterobacteria" MIKROBIOL. ZHURN. Vol. 49 No 6, 1987 pp 83-85.

7. I. Ya. Zakharova, N. V. Tanatar, "Lipopolysaccharides of *Pseudomonas*" MIKROBIOL. ZHURN. Vol 46 No 6, 1984 pp 78-92.

8. N. I. Pendus, R. I. Gvozdyak, S. Z. Ayzenberg, "Bacterial Diseases of Ginseng" *2yu Resp. konf. po meditsinskoy botanike (tezisy dokladov)* [Second Republic Conference on Medical Botany (Summary of Reports)] Kiev, 1988 p 146.

9. M. A. Soldatkina, Yu. A. Knirel, N. V. Tanatar, I. Ya. Zakharova, "Immunological and Structural Studies of the Lipopolysaccharides of *Pseudomonas cepacia*" MIKROBIOL. ZHURN. Vol 51 No 2, 1989 pp 32-38.

10. S. F. Khodos, "Agents of Bacterial Diseases of Carrots in Storage" *Fitonsidy. Bakterialnyye bolezni rasteniy* [Phytoncides. Bacterial Diseases of Plants] Uzhgorod, Oct 1985 (Summary of Reports) Kiev: Nauk. dumka, 1985 part 2 pp 72-73.

11. *Bergey's Manual of Determinative Bacteriology* first ed., Baltimore, London: The Williams and Wilkins Co. 1984 Vol 1 pp 469-476.

12. B. L. Biran, E. W. Gardner, "A Simple Procedure for Detecting the Presence of Cyclopropane Fatty Acids in Bacterial Lipids" APPL. MICROBIOL. Vol 16 No 4, 1968 pp 549-552.

13. E. Duveiller, "La pourriture bacterienne de la chicoree witloof causee par *Pseudomonas cichorii* au Burundi" PARASITICA Vol 42 No 2, 1986 pp 55-57.

14. S. C. Gouk, M. J. Noonan, D. R. Musgrave, "Identification of *Pseudomonas cichorii* by Enzyme-Linked Immunosorbent Assay (Elisa)" *Proc. 7th Int. Conf. Plant Path. Bact.* (Budapest, Hungary, 1989) Plant Pathogenic Bacteria, Budapest 1989 pp 877-882.

15. E. Grasset, "Sur l'endotoxine typhique obtenue par congelation repetee CR5" BIOL. Vol 118, 1935 p 765.

16. R. G. Grogan, I. J. Misaghi, K. A. Kimble et al., "Varnish Spot, Destructive Disease of Lettuce in California Caused by *Pseudomonas cichorii*/Phytopathology Vol 67 No 8, 1977 pp 957-960.

17. J. D. Janse., "Biology of *Pseudomonas cichorii* in Chrysanthemum" BULL. OEPP Vol 17 No 3, 1987 pp 321-333. 18. C. W. Moss, S. B. Samuels, J. Laddle, R. M. McKinney, "Occurrence of Branchedchain Hydroxy Fatty Acids in *Pseudomonas maltophilia*" J. BACTERIOL. Vol 14 No 3, 1979 p 1018.

19. O. Ouchterlony, "Diffusion in Gel Methods for Immunological Analysis" PROGR. IN ALLERGY, 1958 p 1-85.

20. N. Rivera, Z. Amat, M. Hevesi, "Pudricion foliar del pimiento en Cuba Causada pro *Pseudomonas cichorii*" AGROTECN. CUBA Vol 13 No 2, 1981 pp 67-72.

21. D. E. Stead, "Grouping of Plant-Pathogenic and Some Other *Pseudomonas* spp. By Using Cellular Fatty Acid Profiles" J. SYST. BACT. Vol 42 No 2, 1992 pp 281-295.

22. D. B. Swingle, "Center rot of 'French Endive' or Wilt of Chicory (*Cichorium intybus*)" PHYTOPATHOLOGY Vol 15 No 11, 1925 p 730.

23. H. H. Thornberry, H. W. Anderson, "Some Bacterial Diseases of Plants in Illinois" PHYTOPATHOLOGY Vol 27, 1937 pp 946-949.

24. M. F. Widal, "Serodiagnostic de la fievre typhoide" BULL. MEM. SOC. MED. HOP. SER. Paris Vol 13, 1896 p 56.

25. S. G. Wilkinson, L. Galbraith, G. A. Lightfoot, "The Cell Wall Lipids and Lipopolysaccharides of *Pseudomonas* species" EUR. J. BIOCHEM. Vol 33 No 1, 1973 pp 158-174.

Russia: Attempts at Creating a Vaccine Against Ebola Fever

964D0769A Moscow VOPROSY VIRUSOLOGII in Russian Vol 40 No 6, Nov-Dec 95 pp 257-260

[Article by A. A. Chepurnov, I. V. Chernukhin, V. A. Ternovoy, N. M. Kudoyarova, N. M. Makhova, M. Sh. Azayev and M. P. Smolina, Vektor Virology and Biotechnology State Science Center, Koltsovo, Novosibirsk Oblast; (manuscript received 2 Dec 94) UDC 615.371:578.833].012]

[FBIS Translated Text] The Ebola fever is a contagious, highly lethal disease [1]. The exotic character and

rareness of this disease do not lessen the need for specific prevention agents and the discovery of new Ebola-like viruses (Reston, Pennsylvania strains) [11, 13, 16, 17], having an unknown pathogenic potential, intensifies its significance.

After the isolation of the Ebola virus as the etiologic factor of this disease, scientists repeatedly made attempts to obtain an agent for its specific prevention. First of all attempts were made to create a whole-virion inactivated vaccine. In 1978 it was postulated in [12] that since inactivated vaccines against hemorrhagic fevers caused by arenaviruses are effective, similar vaccines might also be effective against the Ebola fever. A standard scheme was proposed for obtaining an inactivated vaccine and the creation of such a preparation was expected after 2-3 years. In actuality, during past years a rather great many attempts have been made to use inactivated preparations for vaccination. The opinions of authors who have carried out such studies differ diametrically. For example, G. Lange, et al. [14] immunized primates with concentrated purified Ebola virus inactivated by γ-irradiation using a bacterial adjuvant. On the basis of the results the authors expressed doubts concerning the possibility of induction of immunity by means of inactivated proteins. At the same time H. Lupton, et al. [15] demonstrated the presence of partial protection against this infection in immunized guinea pigs and V. V. Mikhaylov, et al. [5] obtained well-expressed protection for hamadryas baboons when using a concentrated inactivated virus for immunization. The contradictory nature of the data in the literature can be attributed to different factors, but it is evident that the possibility for creating an effective inactivated preparation for prevention of the disease is indisputable.

We designed and tested several types of whole-virion inactivated preparations. However, in the tests we did not obtain reliable protection of the laboratory animals immunized with these preparations against the Ebola virus. In the course of the experiments studies were made not only of the protective properties of different types of Ebola virus preparations, but also the special features of the immune response of the animals to the administration of both the killed and live virus. The results are presented in this article.

Materials and methods. The Ebola virus, Zaire strain, was obtained from the national collection of the Virology Center, Microbiology Scientific Research Center, RF Ministry of Defense, used for the preparation of inactivated whole-virion preparations, as well as for the infection of primates.

We obtained the Ebola virus, strain 8 m.s., by adaptation of the Zaire strain to guinea pigs by means of successive passages in these animals. Initially the Zaire strain had low virulence for this species of laboratory animals, which does not make possible their use as a laboratory model of infection.

The virus was adapted by means of selective successive passages of the initial strain in guinea pigs [10]. For this purpose a group of animals was administered 0.5 ml of a 10 percent suspension of a liver homogenate of a rhesus monkey which had died after infection by the Zaire strain. Some of the guinea pigs developed a nonlethal infection accompanied by an increase in body temperature (to 40°C) and viremia; the next group was infected by a 10 percent liver suspension from these animals. For subsequent inoculation use was made of specimens with a maximum temperature reaction which increased from passage to passage. After the third passage the appearance of lethal outcomes was noted. In the inoculation process the capacity of the virus to multiply in the liver of the guinea pigs gradually increased from 2.9+/-0.4 to 5.5+/-0.7 lg plate-forming units per 1 ml of 10 percent homogenate. The LD_{50} and ID_{50} for the guinea pigs increased up to the 8th passage and attained 6.5+/-0.7 and 7.5+/-0.7 lg respectively, after which they virtually did not change. With infection by viral material of late passages (8th-11th) the guinea pigs, after 4-7 days of incubation, developed a feverish state lasting for about 4 days. In many cases the fever had a two-wave course with peaks on the 4th-7th and 11th-13th day. On these days a maximum content of the virus was observed in the organs. The percentage of death of the animals increased from passage to passage and there also was a decrease in their lifetime. In the late passages the animals usually perished on the 7th-9th day. The temperature reaction also was less expressed in the early passages; the maximum temperature rise attained 39.8-40.0°C, but in the 6th-11th passages it rose to 41.5-42.0°C. Prior to the death of the animal the temperature decreased critically to 35.5-37.0°C. The animals rapidly lost weight. Anorexia was noted. At the height of the disease and especially prior to death the coordination of movements was impaired. In many cases diarrhea appeared 2-3 days prior to the death of the guinea pigs. Symptoms of intestinal hemorrhaging were observed.

The pathologic anatomy picture observed in the autopsy of the animals infected by the virus in the late passages differed from that when using an unadapted virus primarily in that the liver and spleen were distinctly hypertrophied and had a clayey, sometimes spotty coloring. By the 8th passage the influence of age (mass) of the infected animal on sensitivity to the causative agent had smoothed out. Whereas in the early passages guinea pigs with a weight 180-200 g had the maximum sensitivity, by the 8th passage animals of any weight were identically sensitive to the virus.

However, there was a substantial decrease in the virulence of the resulting strain for newborn common white mice. For example, whereas a suspension of the initial virus with a titer 5.8 lg plate-forming units/ml contained 6.66 lg LD_{50}/ml for the newborn mice, the virus material of the 8th passage with this same titer contained 2.28 lg LD_{50}/ml.

The specificity of the resulting strain was confirmed serologically, as well as by electron microscopy, the results of electrophoresis and the RNA sequence. In its antigen properties the resulting strain did not differ from the initial level. The stability of properties of the resulting strain was checked in 7 passages in a culture of Vero cells and 1 passage in hamadryas baboons, which did not result in a loss of properties. The strain was designated 8 m.s. The strain was cloned by triple sampling of negative colonies under an agar covering. The resulting clones did not differ significantly from 8 m.s. Clone 4 of strain 8 m.s. was used in this study for the infection of immunized guinea pigs.

Table 1. Protective Properties of Whole-Virion Inactivated Preparations

Preparation	Species and Number of Laboratory Animals	Infecting Dose, LD_{50}	Number of Surviving Animals
1	Hamadryas, 7	10-20	0
	Guinea pigs, 10	10-20	2
2	Hamadryas, 4	10-20	0
	Guinea pigs, 10	10-20	1
3	Hamadryas, 10	10-20	0
	Guinea pigs, 10	10-20	5
4	Hamadryas, 5	10-20	0
	Guinea pigs, 10	10-20	2
	Same	100-200	0

Animals. Guinea pigs weighing 200-250 g, hamadryas baboons weighing 3-5 kg, chinchilla rabbits weighing 2.5-3.5 kg and common white mice 1-2 days old were used. The animals were obtained from the vivarium of the Vektor Virology and Biotechnology State Science Center and were kept on a standard ration. All painful procedures were carried out after the administration of painkillers.

The biologic titer of the Zaire strain was determined using mice 1-2 days old; the strain 8 m.s. was determined using guinea pigs. Both strains also were titrated by the method of negative colonies under an agar covering [20].

The following preparations were prepared on the basis of the Zaire strain for studying the efficacy of the inactivated vaccines:

1) a suspension from the brain of infected newborn mice. The baby mice were infected intracerebrally with 0.03 ml of virus-containing culture fluid (VCF) with a titer 2.0×10^8 plate-forming units/ml. On the 8th-10th day after infection the brain was extracted, a 10 percent suspension was prepared and it was clarified by low-speed centrifuging. The biologic titer was 3.0×10^8 plate-forming units/ml.

2) a VCF of a monolayer of a culture of L-68 cells. The VCF was collected on the 7th day after infection of the monolayer with a dose 0.01 plate-forming unit/cell. The biologic titer of VCF was 4.0×10^8 plate-forming units/ml;

3) an extract from a homogenate of chicken embryos infected in a dose $n \times 10^7$ plate-forming units/embryo designed in such a way that it contained both intact virions and also fragments of the cell membrane with a gemmating virus. The biologic titer was 2.0×10^8 plate-forming units/ml;

4) a preparation obtained by ultrafiltration of VCF and ultracentrifuging in a sucrose density gradient. The electrophoretic purity was 95 percent. The physical titer was $n \times 10^{11}$ virions/ml [3, 6, 8].

The enumerated preparations were inactivated by formalin in a final concentration 0.05 percent over the course of 24 hours at 37°C with mixing and then over the course of 3 days at 4-6°C. The absence of residual infectiousness was checked by intracerebral administration to newborn white mice with subsequent blind passages.

The inactivated whole-virion preparations were sorbed on aluminum hydroxide. Immunization was carried out twice — on days 0 and 21. In each immunization preparation 4 was administered to guinea pigs in a dose 0.2 ml and to hamadryas baboons in a dose 1 ml, which corresponded to 1-3 and 30 and 100 μg. The animals were infected 21-23 days after a second intramuscular immunization with VCF in a dose 10-20 LD_{50} for the corresponding species of animals.

The neutralization reaction (NR) was carried out by incubating a virus-serum mixture for 18 hours at 4-6°C. The neutralization index was determined as the difference of the logarithms of the virus titers in the experiment and in the control.

A solid-phase immunoassay was carried out in conformity to a method described earlier [3,4].

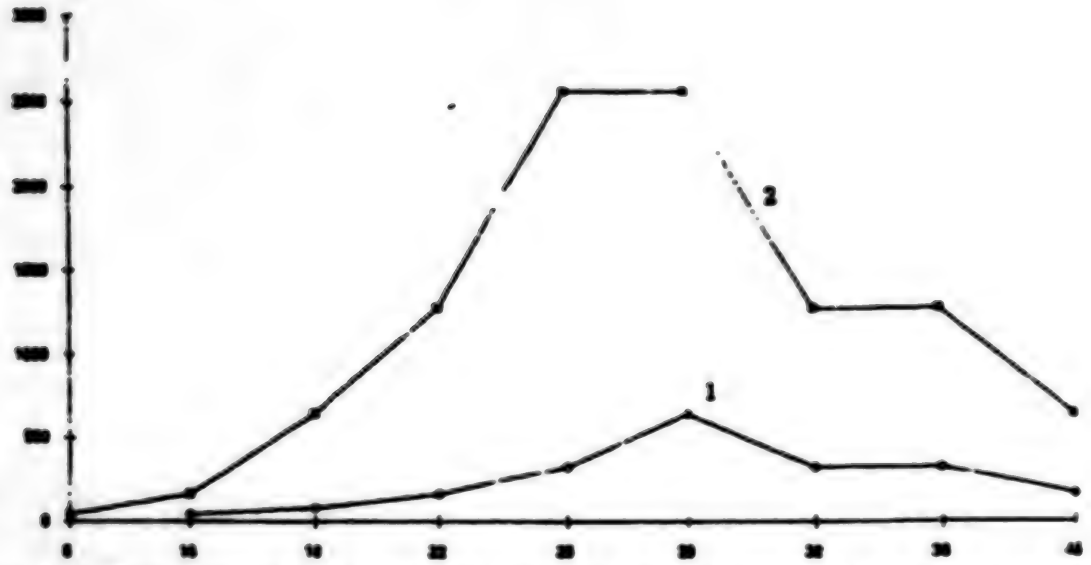
Results and Discussion. The results of study of the protective properties of the inactivated whole-virion preparations are represented in Table 1. It is shown that we could obtain some protective effect in guinea pigs when using the preparation most saturated with the antigen, which corresponds to data in the literature [15]. However, a protective effect was observed with an infecting dose 10 LD_{50}, whereas when using doses of 100 and 1,000 LD_{50} all the immunized animals perished. The used preparations did not give a protective effect when using hamadryas baboons, a more sensitive model. In this respect our results differ from the data published by V. V. Mikhaylov, et al. [5]. Since we used preparations similar in their formulation, it can be assumed that a positive effect was attained due to use of Freund's adjuvant and the large quantities of antigen administered during immunization.

We made attempts at another approach for creating agents for the specific prevention of the Ebola fever. It was demonstrated experimentally that the administration of increasing doses (10, 100, 1,000 plate-forming units) of the Zaire strain (nonlethal for guinea pigs) to guinea pigs led to the formation in the latter of an immunity impeding the development of the disease when injury is received from high doses of the lethal strain (8 m.s.). In such a case the protection index attained 4.5 lg LD_{50}. These results give definite hopes for the possibility of creating a highly efficacious preparation for prevention of the Ebola fever, but for further progress in this direction it is necessary to understand the mechanism of immunopathogenesis of the Ebola disease and the mechanism of the immune reaction in response to antigen administration.

It was noted in the course of the experiments that the titers of antibodies to the Ebola virus (determined in an immunoassay) during immunization of the animals with inactivated preparations were greater than in immunization with the live virus, that is, in this disease the antibodies are not a reliable indicator of the level of protection. We carried out a number of experiments for studying the reactions of cellular [2, 7, 9] and humoral immunity of the body when the Ebola virus was injected. For this purpose rabbits (animals insensitive to this causative agent) were administered equal doses (100 μg) of live and killed virus. The dynamics of change in the titers of antibodies in the serum of the animals was studied in immunoassays. The sera obtained upon completion of the immunization cycle were studied in the NR.

In rabbits immunized by the live Ebola virus (group 1) the antibodies were detected in an immunoassay on the 18th day after the onset of immunization (see figure). In rabbits which had been administered killed viral material (group 2) antibodies already appeared on the 8th day after the onset of immunization.

Repeated immunization caused a further increase in the titers of antibodies in the blood serum of group-2 animals. In group-1 animals the antibodies were registered at later times and in lower titers. The antibody titers in the blood of group-2 animals also were 5-6 times greater than the antibody titers in group-1 animals.



Dynamics of titers of antibodies to Ebola virus in serum of rabbits immunized by live (1) and killed (2) virus. Along y-axis — serum titer (in quantities inverse of dilutions); along x-axis — time after immunization (in days).

On the 35th day after immunization a serum was obtained from the animals and studied for virus-neutralizing activity (Table 2). In this case the opposite tendency was detected. In rabbits immunized with the live virus the neutralization index (in the NR) was 5-10 times higher than for those immunized by the killed virus. Similar NR data were obtained for guinea pigs after their immunization by increasing doses of the live virus (Zaire strain) or a dose of killed virus increased to 30 μg. This phenomenon can be attributed to the fact that with immunization by the live and killed virus the sera obtained contain antibodies reacting with different antigen determinants of the virus. In actuality, in the subsequent analysis of the sera of rabbits in the radioimmunoprecipitation reaction we established that they differ with respect to presence of antibodies to the virus proteins Vp24 and Vp40 in animals immunized with the live virus, whereas in the animals immunized with inactivated material the serum did not precipitate these proteins.

Table 2. Neutralization Indices (in $\log_2$) for Ebola Virus With Immune Sera of Rabbits and Guinea Pigs

NR Test Method	Rabbit Serum		Guinea Pig Serum	
	Immunization			
	Live Virus	Killed Virus	Live Virus	Killed Virus
In nonlinear newborn white mice	3.0+/-0.6	0.3+/-0.5	5.0+/- 0.4	1.0+/-0.6
In culture of Vero cells	4.0+/-0.5	1.0+/-0.7	5.0+/-0.5	0.5+/-0.6

The collected data make it possible to postulate that the virus-neutralizing activity of the antiserum in animals inoculated with the live Ebola virus is exerted by means of blocking of the virus proteins Vp24 and Vp40, which probably have an important function in the process of replication of the virus in the body.

It is possible that the immunogenicity of these proteins is realized as a result of expression on the surface of a host cell in the course of replication, whereas in collected form they can be blocked by other proteins. Accordingly, the obtaining of an immune response against individual virion peptides, being a key factor

in the vital functioning of the virus, will possibly play a significant role in solving the problems involved in specific prevention of the Ebola fever.

On the other hand, it is not impossible that the absence of virus-neutralizing activity in the serum obtained for the killed virus is associated with denaturation in the process of inactivation of antigen determinants inducing the production of neutralizing antibodies.

On the basis of what has been said we feel that the creation of an attenuated or recombinant vaccine, reproducing native immunogenic proteins in the body, will ensure a more effective protection against infection in comparison with an inactivated vaccine.

The collection of preparative quantities of Ebola virus enabled us to isolate virus RNA and obtain a library of E. coli clones carrying copies of virus RNA in the cDNA plasmids pBR322 [18, 19]. This created a basis for obtaining a recombinant vaccine on the basis of the ospovaccine virus and genes coding immunogenic proteins of the Ebola virus.

The work was done with the financial support of the Russian Fund for Fundamental Research (project 93-04-06712).

Bibliography

1. Virusnyye gemorragicheskiye likhoradki: Doklad komiteta ekspertov VOZ (Viral Hemorrhagic Fevers: Report of WHO Committee of Experts), Moscow, 1986.

2. Volchkov, V. Ye., Ignatyev, G. M., Blinov, V. M. and Chepurnov, A. A., in: Rossiyskaya nauch. konf. po genetike i biokhimii osobo opasnykh vozbuditeley infektsionnykh zabolevaniy (Russian Scientific Conference on Genetics and Biochemistry of Especially Dangerous Causative Agents of Infectious Diseases), Volgograd, p 32, 1992.

3. Merzlikin, N. V. and Chepurnov, A. A., Immunologiya i spetsificheskaya profilaktika osobo opasnykh infektsiy (Immunology and Specific Prevention of Especially Dangerous Infections), Saratov, p 273, 1993.

4. Merzlikin, N. V., Chepurnov, A. A. and Istomina, N. N., et al. VOPR. VIRUSOL. (Problems in Virology), No 1, pp 31-35, 1995.

5. Mikhaylov, V. V., Borisevich, I. V., Chernikova, N. K., et al., IBID., No 2, pp 82-84, 1994.

6. Tikhonov, V. Ya., Kotov, A. N., Volchkov, V. Ye., et al., in: Izucheniye i profilaktika osobo opasnykh virusnykh infektsiy (Study and Prevention of Particularly Dangerous Viral Infections), Koltsovo, p 9, 1993.

7. Chepurnov, A. A., Volchkov, V. Ye., Kudoyarova, N. M., et al., in: Immunologiya i spetsificheskaya profilaktika osobo opasnykh infektsiy, Saratov, p 211, 1993.

8. Chepurnov, A. A., Merzlikin, N. V., Ryabchikova, Ye. I., et al., VOPR. VIRUSOL., No 6, pp 254-257, 1994.

9. Chepurnov, A. A., Volchkov, V. E. and Ignatyev, G. M., in: International Congress of Virology, 9-th, Glasgow, p 300, 1993.

10. Chepurnov, A. A., Smolina, M. V., Kudojarova, N. M., et al., IBID., p 300.

11. Fisher-Hoch, S. P., Brammer, T. L., Trappier, S. G., et al., J. INFECT. DIS., Vol 166, No 4, pp 753-763, 1992.

12. Gerald, A. E. and Francis, E. C., Ebola Virus Haemorrhagic Fever, edited by S. R. Pattyn, Amsterdam, New York, 1978.

13. Jahrling, R. B., Geisbert, T. W., Dalgord, D. W., et al., LANCET, No 8688, pp 502-505, 1990.

14. Lange, G. V., McCormic, G. B., Walker, D. H., et al., in: American Society of Microbiology; Annual Meeting: Abstracts. Las Vegas, p 295, 1985.

15. Lupton, H. W., Lambert, R. D. and Bumgardner, D. L., LANCET, Vol 13, pp 1294-1295, 1980.

16. Schaefer, E., NATURE, Vol 630, p 380, 1990.

17. Vikal haemorrhagic in imported monkeys, WKLY EPIDEMIOL. REC., Vol 67, No 19, pp 142-143, 1992.

18. Volchkov, V. Ye., Blinov, V. M. and Netesov, S. V., FEBS LETT., Vol 305, No 3, pp 181-184, 1992.

19. Volchkov, V. Ye., Blinov, V. M., Kotov, A. N., et al., in: International Congress of Virology, 9th, Glasgow, p 299, 1993.

20. Yones, D. M., Lamber, R. D. and Gupton, H. N., J. CLIN. MICROBIOL., Vol 13, No 4, p 791, 1981.

Russia: Development and Study of Properties of Immunoglobulin Against Ebola Fever

964D0769B Moscow VOPROSY VIRUSOLOGII in Russian Vol 40 No 6, Nov-Dec 95 pp 270-273

[Article by I. V. Borisevich, V. V. Mikhaylov, V. P. Krasnyanskiy, V. N. Gradoboyev, Ye. V. Lebedinskaya, N. V. Potryvayeva and G. D. Timankova, Virology Center, Microbiology Scientific Research Institute, RF Ministry of Defense, Sergiyev Posad; (manuscript received 16 Feb 95) UDC 616.98:578.8]

[FBIS Translated Text] The Ebola virus, known since 1976 [2], is a representative of the family of

phyloviruses and belongs to the category of particularly dangerous pathogens, in humans causing a severe fever-ish contagious disease with a hemorrhagic syndrome and high lethality, attaining 88 percent [11].

Table 1. Characteristics of Preparations of Ebola Immunoglobulin (data from 23 series)

Index, Measurement unit	Required Index	Index Obtained
Transparency (optical density at wavelength 540+/-10 nm), optical density units	0.05	0.01-0.05
Chromaticity (optical density at wavelength 400+/-5 nm), optical density units	0.15	0.03-0.15
pH	7.0-7.5	7.0-7.5
Total quantity of protein, %	10+/-1	9.0-11.0
Content of γ-globulin fraction, %	90	90-98
Content of albumins, α- and β-globulins, %	10	2-10
Residual quantity of ethyl alcohol, %	4	0.9-3.1
Specific activity, VNA titer	-	1:4,096-1:65,536
Pyrogenicity	Apyretic	Apyretic
Toxicity	Nontoxic	Nontoxic
Sterility	Sterile	Sterile
Useful life	Up to 3 years	3 years

The epidemiology, patho- and immunogenesis of the Ebola fever have not yet been studied adequately. There is a lack of both specific and aspecific preventive and therapeutic agents. The affliction of man with hemorrhagic Ebola fever is possible not only with infection in endemic regions (equatorial regions of Zaire and Sudan), but also when carrying out scientific research work [17] and also as a result of contact with imported monkeys [18]. In 1980 H. Lupton, et al. [19] obtained a vaccine on the basis of the Ebola virus inactivated by β-propiolactone after cultivation in a culture of Vero cells, having a low efficacy in an experiment on guinea pigs.

An attempt to create a whole-virion inactivated vaccine against the Ebola fever at the Vektor RF State Science Center for Virology and Biotechnology (Koltsovo) also did not yield positive results. The authors concluded that there were no prospects for obtaining such a preparation [14]. The experience in developing an inactivated concentrated purified vaccine against the Ebola virus accumulated at the RF Virology Center, Microbiology Scientific Research Institute (VTs NIIM), Ministry of Defense, Sergiyev Posad) indicated that there must be a more thorough study of the structure of the virion, mechanisms of patho- and immunogenesis, with the obtaining of an immunologically fully effective antigen of the Ebola virus [8].

However,the conducting of research for study of the virus, pathogenesis of the disease and development of an effective vaccine against the Ebola virus is being held back by the high danger of infection of personnel working with the Ebola virus. A case of intralaboratory infection of a specialist at the Microbiology Center in Porton (England) has been described [17]. The patient was treated with the plasma of reconvalescents and interferon.

However, the supplies of such plasma are limited (it is lacking in Russia) and its administration involves the risk of infection of persons with the viruses of hepatitis, leukemia, human immune deficiency syndrome and other causative agents of infectious diseases transmitted through the blood. The hyperimmune horse serum, containing virus-neutralizing antibodies (VNA) to the Ebola virus in high titers (1:4,096), obtained at the VTs NIIM, is without the shortcomings inherent in human immune plasma and is a real substrate for the preparation of immunoglobulin preparations [5].

The objective of this study was obtaining an immunoglobulin against the Ebola fever (Ebola immunoglobulin) and an assessment of its properties.

Materials and methods. The Zaire strain of the Ebola virus, obtained from the National Collection of Viruses of Hemorrhagic Fevers of the First Pathogenicity Group, VTs NIIM, was used.

The Ebola immunoglobulin was obtained from hyperimmune horse sera [5] by the Cohn alcohol cold fractionation method [16].

The physicochemical and immunobiologic properties of the specific preparation were studied in accordance with the requirements of the RF Ministry of Health and the Medical Industry and the National Oversight Agency [4, 9, 10, 13].

In a comparative study of the sensitizing properties of the collected immunoglobulin use was made of the γ-, β-globulins against Japanese encephalitis from horse serum (series No 41, control No 2963), produced by the NPO Virion, and immunoglobulin against Venezuelan equine encephalitis from horse serum (series No 15, control No 348), produced at the VTs NIIM.

In the experiments use was made of hamadryas baboons (Papio hamadryas) weighing 3-9 km, chinchilla rabbits weighing 1.5-2 kg, guinea pigs weighing 200-250 g and common white mice weighing 17-20 g obtained from the VTs NIIM vivarium during the period from 1988 through 1993.

The monkey was infected intramuscularly with a culture of the Ebola virus (in a dose 10-29 LD_{50} for the particular species of monkeys), diluted in a Hanks solution with 2 percent cattle blood serum and antibiotics (200 IU of penicillin and streptomycin each); the volume of the inoculate was 1 ml.

Clinical observations were made of the infected animals with daily measurement of rectal temperature.

The concentration of the Ebola virus in samples of the blood and liver of the monkeys was determined by titration in a multilayer culture of 6619-1 (D) cells (cell donor — kidney of embryo of green African marmoset) by the negative colonies method.

Monolayer cultures of 6619-1 (D) and SMK-AN-1 (D) cells (cell donor — kidney of green African marmoset) were used in setting up the neutralization reaction (NR) by the plate formation suppression method (during determination of the VNA titer in immunoglobulin preparations). The surviving monkeys were subjected to euthanasia by the intravenous administration of 0.5 g of hexanal dissolved in a physiologic solution of sodium chloride (in 1-g flasks of the drug produced by the PO Olaynfarm).

The statistical processing of the data was carried out in accordance with generally employed methods [1].

Results and Discussion. A laboratory study of the immunoglobulin obtained from horse blood serum indicated its correspondence to the requirements imposed on heterologous immunoglobulins (Table 1).

An assessment of the sensitizing properties of the Ebola immunoglobulin when determining hypersensitivity of the immediate type by means of reproduction of the anaphylaxis syndrome in guinea pigs [9], as well as using the index of destruction of leukocytes in the leukocytolysis reaction [3] in experiments on hamadryas baboons, made it possible to conclude that a preparation based on these indices does not differ from the commercial immunoglobulins from the blood serum of horses. The pharmacokinetics of the drug was studied for choosing the tactics for use of the Ebola immunoglobulin in the urgent prevention of the Ebola fever in hamadryas baboons.

The animals were intramuscularly administered immunoglobulin with a VNA titer to the Ebola virus 1:65,536 in a dose 6 ml and the dynamic level of the specific antibodies in the blood was determined.

It follows from the collected data that the VNA is present in the blood of the monkeys for 10 days after immunoglobulin administration. The maximum level of antibodies (1:128-1:512) falls in the period from 30 minutes to 1 day after administration of the drug; then the concentration of antibodies in the blood of these monkeys is reduced and on the 14th day VNA are not determined in the blood serum of the animals. The efficacy of the Ebola immunoglobulin was studied in hamadryas baboons with an experimental form of the fever. The immunoglobulin was administered in a dose of 6 ml in both preventive and in urgent prophylactic schemes.

As a result of the research it was established that there is a dependence between the efficacy of the drug and the scheme for its administration and specific activity.

An increase in the incubation period (the time prior to appearance of a fever), considerable decrease in the gravity of the course of the infection, absence of a hemorrhagic rash, increase in the lifetime of diseased animals and decrease in the level of virusemia at early times in the course of the disease in comparison with similar indices in animals of the control group are attained by the earliest possible administration of immunoglobulin (Table 2).

Table 2. Assessment of efficacy of Ebola immunoglobulin with intramuscular infection of monkeys by Ebola virus

Time of immunoglobulin administration	VNA titer in immunoglobulin	Number of monkeys used in experiment	Number of monkeys survived, %	Incubation period for sick monkeys (mean X+/-s), days	Lifetime of deceased monkeys, (mean X+/-s), days	Percentage of animals with viremia on days 5-6th	7-8th	10-11th	13-15th	20-33d
2 hours before infection	1:8,192	2	100	-	-	0	0	0	0	0
Minutes after infection:										
5-15 minutes	1:4,096	6	50	9+/-4	18+/-9	33	0	0	40	0
	1:8,192	-	-	-	-	-	-	-	-	
	1:65,536	10	100	-	-	0	0	0	0	0
30 min	1:4,096	5	0	7+/-1	10+/-1	-	100	100	-	-
	1:8,192	-	-	-	-	-	-	-	-	-
	1:65,536	14	80	11	14+/-2	0	0	21	0	0
60 min	1:4,096	5	20	9+/-4	11+/-5	-	40	50	50	0
	1:8,192	-	-	-	-	-	-	-	-	-
	1:16,384	5	100	-	-	0	0	0	0	0
120 min	1:4,096	3	0	9+/-3	13+/-2	-	100	100	-	-
	1:8,192	-	-	-	-	-	-	-	-	-
	1:16,384	7	29	10+/-2	26+/-11	0	14	43	67	0
Preparation not administered (control)	-	20	0	6+/2	9+/-1	100	100	100	-	-

The greatest protective effect from the administration of Ebola immunoglobulin was observed with a VNA titer in the drug 1:8,192-1:65,536. The administration of Ebola immunoglobulin with a VNA titer 1:8,192 and above iv a dose of 6 ml for 1 hour after intramuscular infection of hamadryas baboons with the Ebola virus resulted in a complete absence of the virus in the blood during the entire time of observation, its absence in the liver of the surviving animals and with a virtually complete (up to 100 percent) protection of the infected monkeys.

The phenomenon of efficacy of the specific immunoglobulin at early times after infection in all probability is associated with neutralization of the Ebola virus in vivo up to the moment of interaction of the virus with the sensitive receptors of the host cell. Evidently for this reason the concentration of the Ebola virus in the liver of the deceased experimental and control monkeys was approximately identical.

The Ebola virus for the first time was determined in the cells of the system of mononuclear phagocytes in the body of an infected animal after 48 hours [12]. The specific VNA to the Ebola virus are already determined in the blood of hamadryas baboons 30 minutes after administration of the Ebola immunoglobulin to the animals, attain a maximum titer after 1 hour and circulate over the course of 10 days. Over a period of 1 hour there is a neutralization of the Ebola virus in vitro when setting up a neutralization reaction with the specific immunoglobulin.

This evidently explains the absence of an effect from goat (sheep) immunoglobulin against the Ebola fever when studying its efficacy [6, 7], since the specific preparation with a low VNA titer was administered to the animals after 2-4 hours or 1-3 days.

At the present time the dependence between the level of antibodies after active or passive immunization and resistance to infection in a number of viral infections is unquestionable [15]. The results which we obtained confirm this regularity. However, the use of Ebola immunoglobulin has well-expressed special features which are evidently attributable to the complexity of pathogenesis of the disease. Only the earliest possible (within 1 hour after infection) administration of a preparation with a high VNA content (1:8,192) makes it possible to achieve a positive result.

The administration of immunoglobulin at later times results in a worsening of the infectious process, as also was observed when using goat (sheep) immunoglobulin [7]. This possibly was attributable to the impact exerted on the body by the forming immune antigen-antibody complexes [12].

Thus, as a result of the research conducted by the Cohn alcohol method using horses immunized by the Ebola virus it was possible to obtain a specific immunoglobulin with a VNA titer to the Ebola virus 1:4,096 or more, not differing in its properties from commercial heterologous immunoglobulins. The conducted laboratory-experimental study of the preparation made it possible to validate effective tactics for use of the developed immunoglobulin.

Bibliography

1. Ashmarin, I. P. and Vorobyev, A. A., Statisticheskiye metody v mikrobiologicheskikh issledovaniyakh (Statistical Methods in Microbiological Research), Leningrad, 1962.

2. Virusologiya. T 1 (Virology. Vol 1), edited by B. Fields, et al., Moscow, pp 44-45, 1989.

3. Vorobyev, A. A., Afanasyev, S. S., T. Patrikeyev, G. T., et al., ZHURN. MIKROBIOL. (Journal of Microbiology), No 12, pp 21-28, 1978.

4. Gosudarstvennaya farmakopeya SSSR. 11-e izd. (USSR State Pharmacopeia. Eleventh Edition), Moscow, No 2, 1990.

5. Krasnyanskiy, V. P., Mikhaylov, V. V., Borisevich, I. V., et al., VOPR. VIRUSOL. (Problems in Virology), Vol 39, No 2, pp 91-92, 1994.

6. Kudoyarova, N. M., Dedkova, L. M., Sergeyev, N. N. and Chepurnov, A. A., in: Izucheniye i profilaktika osobo opasnykh virusnykh infektsiy (Study and Prevention of Especially Dangerous Viral Infections), Koltsovo, p 33, 1993.

7. Luchko, S. V. and Dadayeva, A. A., IBID., p 32.

8. Mikhaylov, V. V., Borisevich, I. V., Chernikova, N. K., et al., VOPR. VIRUSOL., Vol 39, No 2, pp 82-84, 1994.

9. RD 42-28-8-89. Doklinicheskiye ispytaniya novykh meditsinskikh immunobiologicheskikh preparatov. Osnovnyye polozheniya (RD 42-28-8-89. Preclinical Tests of New Medical Immunobiologic Drugs. Basic Provisions), Moscow, 1989.

10. Rukovodstvo po vaktsinnomu i syvorotochnomu delu (Manual on Vaccines and Sera), edited by P. N. Burgasov, Moscow, 1978.

11. Rukovodstvo po rikketsiozam, hemorrhagicheskim likhoradam i entsefalitam (Manual on Rickets, Hemorrhagic Fevers and Encephalitis), edited by I. K. Musabayev, Tashkent, pp 326-338, 1986.

12. Ryabchikova, Ye. I., Kolesnikova, L. V., Tkachev, V. K., et al., in: Izucheniye i profilaktika osobo opasnykh virusnykh infektsiy, Koltsovo, p 13, 1993.

13. FS 42-344VS-90. Fiziko-khimicheskiye, fizicheskiye i immunokhimicheskiye metody kontrolya meditsinskikh immunobiologicheskikh preparatov (Physicochemical, Physical and Immunochemical Methods for Checking Medical Immunobiologic Drugs). Introduced 1 May 91, Moscow, 1991.

14. Chepurnov, A. A., in: Izucheniye i profilaktika osobo opasnykh virusnykh infektsiy, Koltsovo, p 38, 1993.

15. Shuratov, I. Kh. and Sayatov, M. Kh., Faktory i mekhanizmy protivovirusnogo immuniteta (Factors and Mechanisms of Antiviral Immunity), Almaty, 1985.

16. Cohn, E. J., Strong, L. E. and Hughes, W. L., J. AMER. CHEM. SOC., Vol 68, No 3, pp 459-475, 1946.

17. Emond, R. T. D., Evans, B., Bowen, E. T. W. and Lloyd, G., BRIT. MED. J., Vol 2, No 6068, pp 541-544, 1977.

18. Jahrling, P. B., Geisbert, T. W., Dalgard, D. W., et al., LANCET, Vol 335, No 8688, pp 502-505, 1990.

19. Lupton, H. W., Lambert, R. D. and Bumgardner, D. L., IBID., Vol 13, pp 1294-1295, 1980.

Vergina-Like Strains of Tick-Borne Encephalitis Virus in Russia

964D0769C Moscow VOPROSY VIRUSOLOGII in Russian Vol 40 No 6, Nov-Dec 95 pp 260-264

[Article by V. V. Pogodina, N. G. Bochkova, V. I. Zlobin, L. S. Levina, Yu. P. Dzhioyev, T. I. Dzhivanyan and I. A. Sokolova, Poliomyelitis and Viral Encephalitis Institute imeni M. P. Chumakov, Russian Academy of Medical Sciences; Epidemiology and Microbiology Institute, East Siberian Science Center, Siberian Department, Russian Academy of Medical Sciences, Irkutsk, and Yaroslavl Center, State Committee for Sanitary and Epidemiological Oversight; (manuscript received 10 Feb 95) UDC 578.833.26:578.53].08(470)]

[FBIS Translated Text] The true number of serotypes of the virus of tick-borne encephalitis (TBE) circulating in the territory of Russia and the countries of Europe and Asia remains unclear. The choice of vaccine and diagnostic strains of TBE is based on the concept of circulation of two principal subtypes: eastern (synonyms: Far Eastern, first, persulcatus) and western (synonyms: Central European, second, ricinus). During the last decade the widespread occurrence of the serotype Ayna/1448, also called the fourth or East Siberian serotype [1, 9], was demonstrated. In addition, the presence of other antigen variants of TBE, designated Ural-Siberian and Central Asian variants [4], was detected. In an earlier article we pointed out that the Ural-Siberian, Central Asian and East Siberian serotypes are extremely similar in their genetic characteristics and pathogenicity features to the third TBE serotype — the Vergina serotype [11]. This similarity is manifested in the capacity to cause slowly developing encephalitis in experimentally infected animals (monkeys, hamsters) and in a relatively weak hybridization with deoxyoligonucleotide probes, complementary to the genome of the Sofin strain of the eastern subtype [10]. The Vergina strain was isolated in Greece in 1969 from the brain of a paralyzed kid [12, 13]. No information has been reported on the spread of the Vergina serotype beyond the boundaries of Greece. The similarity which we discovered between the Vergina strain and the strains of the Ural-Siberian, Central Asian and Ayna/1448 serotypes served as a basis for their further comparative study and clarification of the possibility of spread of Vergina-like strains within the boundaries of Russia.

Materials and Methods. TBE strains. Fourteen TBE strains were used. The Sofin strain (eastern serotype) was isolated in 1937 from the brain of a person who had died in the Far East from tick encephalitis (TE). Strain 256 and Pregolya-8 (western subtype) were isolated, respectively, in 1940 in Belarus from the tick *I. ricinus* and in 1986 in Kaliningrad Oblast from the tick *D. pictus*. The remaining strains were isolated from the tick *I. persulcatus* in Yaroslavl Oblast in 1988-1990 (Yar-10, Yar-11, Yar-82, Yar-90, Yar-173, Yar-193), in Leningrad Oblast in 1985 (Sestroretsk-3), Novgorod Oblast in 1986 (Chudovo-2), in Kirgizia in 1986 (Buzuuchuk) and Bashkiria in 1987 (Nugush-1). The Buzuuchuk strain belongs to the Central Asian and the Nugush-1 strain belongs to the Ural-Siberian antigen variants of the TBE. The Sofin and 256 strains underwent more than 50 passages through the brain of white mice. The strains isolated from the ticks were used at the level of 4-6 passages in a culture of SPEV cells and in mice. In addition, use was made of variants of strains Yar-90 and Yar-82 undergoing 8-10 additional passages in mice. The Vergina strain was studied in passage dynamics: after the initial passages in suckling mice and an additional 10-11 passages in a culture of SPEV cells and in mice. Detailed information concerning the strains was presented earlier in [10, 11].

Molecular hybridization of nucleic acids (MHNA). The isolation of total RNA from cerebral preparations of white mice infected with TBE and hybridization experiments were carried out as described in [3, 14]. Use was made of a TBE cDNA probe (Sofin strain) and a set of deoxyoligonucleotide probes complementary to genome sectors of the Sofin strain of the eastern TBE subtype [15] and the Neudorfe strain of the western TBE subtype [4]. Hybridization with cDNA was carried out in "hard" (60 and 65°C in 50 percent formamide) and "soft" (65°C, aqueous solution) conditions. The dislocation of the deoxyoligonucleotide probes, complementary to the genome of the Sofin strain, is indicated below: probe p10 — gene of protein C (nucleotides 379-396), S1prM (642-661), S3-M (837-856), S5-E (1285-1311), P2-ns1 (2461-2478), P131-ns2b (4322-4341), P5-ns4b (7015-7032). The deoxyoligonuclides N2 and N3, complementary to the unique sectors of the Neudorfe strain genome, corresponded: probe N2 — to the gene C (395-412), probe N3 — to prM (620-637).

Antigen characteristics of TBE strains. In the RGA and RTGA procedures use was made of borate-salt cerebral antigens and antigens processed with protamine sulfate in the pH range 6.2-6.6 with 0.4 percent goose erythrocytes, as well as a TE commercial diagnosticum produced by the Tomsk Vaccines and Sera Scientific Research Institute. Concentrated PEG-6000 antigens [1] were prepared for the reaction of diffuse precipitation in agar (RDPA). As the antigens in rocket immune electrophoresis (RIEP) use was made of a cultured virus concentrated by the precipitation of PEG-6000 in two stages: first — by the addition of PEG-6000 up to 10 percent to the clarified virus-containing fluid, second —

by the addition of PEG-6000 up to 22 percent to the supernatant remaining after the precipitation of the first PEG precipitate [7]. RIEP was carried out as described in [2]. The neutralization reaction (NR) was carried out by intracerebral infection of white mice with a mixture of sera diluted 1:8 with 10^n dilutions of the virus; the results were expressed in logarithms of the neutralization index (NI).

In the serologic reactions use was made of paired blood sera of humans collected in Yaroslavl Oblast in the TE epidemic season in 1991-1993, as well as the blood sera of Javan macaques experimentally infected under hexanal narcosis by different TBE strains in a dose 10^6-$10^{6.5}$ LD_{50}/ml; the blood of these animals was collected from the 0 through the 85th day after infection.

Results. Determination of genotype of TBE strain. In the MHNA experiments use was made of hybridization conditions and a set of deoxyoligonucleotide probes making it possible to differentiate TBE genetic variants [4], and specifically hard and soft regimes of interaction with cDNA by a probe of the Sofin strain, probes complementary to the conservative (group A) and variable (group B) sectors of the Sofin strain genome, and probes specific for the western TBE subtype, Neudorfe strain. The Sofin strain actively interacted with all the probes, other than N2 and N3 of the Neudorfe strain (Table 1). The strains 256 and Pregolya-8 were hybridized with all probes of group A and some of the probes of group B, complementary to the Sofin strain, and also interacted with probes of the Neudorfe strain. The Vergina, Chudovo-2, Sestroretsk-3 Nugush-1 and Buzuuchuk strains manifested a great similarity with respect to character of interaction with probes specific for the Sofin strain: they were hybridized with cDNA only in a soft regime, reacted only with some of the probes of group A and with not one of the probes of group B. The differences between these strains were detected using probes for the western TBE subtype: the Vergina, Chudovo-2 and Sestroretsk-3 strains interacted with the N2 and N3 probes, whereas the Nugush-1 and Buzuuchuk strains did not react with them. In accordance with the criteria for the differentiation of TBE genotypes [4], the studied strains were assigned: Sofin to the first TBE genetic variant, Nugush-1 and Buzuuchuk to the third genetic variant, 256 and Pregolya-8 to the fifth genetic variant and Vergina, Chudovo-2 and Sestroretsk-3 to the sixth genetic variant.

Antigen properties of Vergina strain. The set of TBE strains was studied with respect to the level of antigen activity using criteria making it possible to determine antigenically complete (AC) and antigenically defective (AD) variants of the virus. The hemagglutinating and precipitating activity of standardly prepared concentrated viral antigens of different strains whose infectious titers fell in the range 10^7-10^{10} plate-forming units/ml (Table 2) were compared. The Sofin, Yar-10, Yar-11 strains (titer 10^9-10^{10} plate-forming units/ml) behaved as AC variants, manifesting hemagglutinating and precipitating activity. In contrast to this, the strains Vergina, Yar-173, Yar-193 (titer $10^{6.5}$-$10^{7.5}$ plate-forming units/ml), not having the indicated types of antigen activity, were assigned to the AD variants. A change in the antigen activity of the Vergina strain as a function of the duration of laboratory passages and host cells was noted. In early passages through suckling mice the titer of borate-salt hemagglutinating antigens attained 1:128 in the pH range 6.2-6.4. After 11 passages in a culture of SPEV cells and 8 passages through the brain of adult mice the hemagglutinating and precipitating activity decreased sharply, evidence of transformation of the AC phenotype into an AD phenotype. The composition of the antigen structures, synthesizing in the culture of SPEV cells with infection by the Vergina strain (AD variant), had differences from the antigen structures of the Sofin strain [8]. In an analysis of the concentrated culture fluid in the RIEP a "rocket" of cathode precipitate of the Vergina strain was detected irregularly, was small in area and weakly colored in comparison with that for the Sofin strain with high titers of the infectious virus. Cloned variants, forming plates 1-2 mm in diameter, were obtained from the population of the Vergina strain by the plates method in a culture of SPEV cells. The virion antigens of the cloned variants did not form a "rocket" of cathode precipitates in the RIEP or yielded a very small weakly colored cathode precipitate.

However, "rockets" of high- and low-molecular nonvirion (soluble) antigens, moving toward the anode in the RIEP, were discovered regularly in an analysis of preparations of the Vergina strain and its clones, much like for the Sofin strain. In a study of antigens of the strains Yar-173 and Yar-193 in the RIEP it was established that they have a similarity to the Vergina strain. The Yar-90 strain in the first passages after isolation from the ticks had the characteristics of the AD variant; then after 10-11 passages in a culture of SPEV cells and in mice it acquired the AC phenotype.

Cross-antigen links of TBE strains were studied using AC and AD variants of the virus. In singly infected monkeys the strains Sofin and Yar-10 caused rapid formation of antihemagglutinins in a high titer (1:640) to different TBE strains, including the Vergina strains. The AC variant of the Vergina strain also induced the formation of hemagglutinating antibodies to different strains, but with a 4-8-fold difference in the titers of homologous and heterologous antibodies (Table 3). The

AD variant of the Yar-90 strain caused the formation of antihemagglutinins primarily to the Vergina strain (titer 1:160) and in low titers (1:20-1:40) to the Sofin and Yar-10 strains. In the NR the sera of monkeys were tested with the Vergina strain (AD variant) and a set of Yaroslavl TBE strains having the AC phenotype. The virus-neutralizing antibodies induced by the Vergina strain reacted only with the Vergina, Yar-90 and Yar-82 strains, but did not interact with the Sofin, Yar-10 and Yar-11 strains. Among the Yaroslavl strains only the Yar-90 strain induced the formation of virus-neutralizing antibodies to the Vergina strain (Table 4).

Table 1. Interaction between genomes of TBE strains and deoxyoligonucleotide probes specific for western and eastern subtypes of virus

Virus strain	Region and year of isolation	Probes for Sofin strain*						Probes for Neudorfe strain		Genetic type**
		cDNA			S5	group		N2	N3	
		65°C fa+	60°C fa+	65°C fa+		A	B			
Sofin	Far East, 1937	+	+	+	+	4/4	3/3	-	-	I
256	Byelorussia, 1940	+	-	-	+	4/4	1/3	+	+	V
Pregolya-8	Kaliningrad Oblast, 1986	+	+	-	+	4/4	2/3	-	+	V
Vergina	Greece, 1969	+	-	-	+	3/4	0/3	+	+	VI
Chudovo-2	Novgorod Oblast, 1986	+	-	-	+	2/4	0/3	+	+	VI
Sestroretsk-3	Leningrad Oblast, 1985	+	-	-	+	0/4	0/3	+	+	VI
Nagush-1	Bashkiria, 1987	+	-	-	+	1/4	0/3	-	-	III
Buzuchuk	Kirgiziya, 1986	+	-	-	+	1/4	0/3	-	-	III

*Hybridization with a cDNA probe was carried out in the presence (fa+) or in the absence (fa-) of 50% formamide. group A included 4 probes for the conservative sectors of the Sofin strain genome (S1, S5, P2, P131); group B included 3 probes for the variable sectors of the Sofin strain genome (P5, P10, S2).

**The genotype of the strains was determined in accordance with the described criteria [4].

Serologic study of patients. During 1991-1993 in Yaroslavl Oblast a study was made of 82 samples of blood serum from 37 patients, including from 20 patients with clinical diagnoses of TE (focal, meningeal and feverish forms with a two-wave course), 8 patients with an "obliterated" clinical picture of TE and 9 patients with diagnoses of ORZ, ORVI [abbreviations not further identified] and Lyme's disease. In the NR use was made of AD variants of the Vergina and Yar-173 strains reacting specifically with homologous sera and the AC Yar-90 and Sofin variants, by means of which group antigen links were serologically detected. Neutralizing antibodies were found in 23 patients. In these cases three immune response variants were observed: a) seroconversion to all the tested strains; b) seroconversion to one of the strains; c) stable titers of antibodies to different strains in paired sera. For example, "polystrain" seroconversion was observed in patient Yu.: the first serum contained antibodies only to the strain Yar-90 (lg NI 1.8); the second serum exhibited antibodies to the Vergina strain (lg NI 2.2); the third and fourth sera neutralized the strains Yar-90, Vergina, Sofin and Yar-173 (lg NI 3.0, 2.2, 2.3, 2.3 respectively). In the case of "polystrain" seroconversion positive responses were obtained in the NR, immunoassay and RTGA procedure with commercial diagnosticums. For example, in patient N in the immunoassay the titer of antibodies increased from 1:320 to 1:10,240, in the RTGA from 1:10 to 1:40, in the NR with the Yar-90 strain the lg NI were 2.7 and 3.0, with the Yar-173 strain — 1.8 and 2.8.

Table 2. Comparison of Antigenic Activity of TBE Strains

Virus strain	Infectious titer, lg PFU/ml		Titer of viral antigens			RSP	Virus phenotype
	SPEV cell culture	concentrated SPEV cell culture	SPEV cell culture	mouse brain	RDPA		
Vergina*	5-6	7-7.5	0-2-4	0	0.2	-	AD
Vergina**	5-5.5	7.5	4.8	128	4.8	+	AC
Yar-82*	7	8	0.2	0	0	-	AD
Yar-82**	8	9	16-32	128-256	16-32	+	AC
Yar-90*	6-7	9	0.2	0	0	-	AD
Yar-90**	8	9	32	256-512	32	+	AC
Sofia	8-9	9-10	32-64	4,096	32-256	+	AC
Yar-10	6.5-7	9.5	8-32	512-1,024	32-64	+	AC
Yar-11	6.5-7	9.5	16-32	512	32	+	AC
Yar-173	4.5-5	6.5-7	0-2	0	0	-	AD
Yar-193	5-5.5	7-7.5	0-2-4	0-4	0	-	AD

Note: The inverse values of the titer of viral antigens are given; the titer of the precipitating antigen was determined with a homologous immune serum; one asterisk — strains changing characteristics in early passages and two asterisks — late passages.

The "polystrain" immune response was noted with typical clinical TE symptoms. The second immune response variant (selective seroconversion in the NR) was characterized by the appearance of antibodies in a low titer (lg NI 2.0-2.7) to only one strain, most frequently to Vergina, in the second-third sera (Table 5). This was noted with typical and "obliterated" pictures of TE and also in one case of Lyme's disease (mixed infection). Among some of the patients there was an increase in the titer of antibodies in the NR only to the Yar-90 strain.

Table 3. Dynamics of Antihemagglutinins in Blood of Monkeys Infected With TBE Strains

Virus strain	Day after infection	RTGA with antigens of TBE strains		
		Vergina (AC)	Sofia (AC)	Yar-10 (AC)
Sofia (AC)	10	160	320-640	320
	14	640	640	640
Vergina (AC)	7	0	0	0
	14	160	40	40
	30	320	40	40
	60	80	20-40	40
	85	1,280	320	640
Yar-10 (AC)	7	0	20	20
	14	-	160	320
	43	640	640	640
Yar-90 (AD)	7	0	0	0
	14	40	20	0
	45	160	20-40	20

Note: The inverse values of the titer of antihemagglutinins are given.

According to NR data, in Yaroslavl Oblast antibodies to the Vergina strain were discovered in 23.1 percent of the population, in 17.5 percent — to the Yar-90 strain, in 13.6 percent — to the Sofia strain and in 9.3 percent — to the Yar-173 strain.

Table 4. Spectrum of Virus-Neutralizing Antibodies in Monkeys Infected by Different TBE Strains

Infected strain of virus	Day after infection	TBE strain in NR, lg NI					
		Vergina	Sofia	Yar-10	Yar-11	Yar-90	Yar-82
Vergina (AD)	30	2.6	0	0	0	2.0	2.4
	43	2.4	0	0	0	2.0	2.0
	57	2.6	0	0	0	2.3	2.0
	85	3.1	0	0	2.0	2.9	3.0
Yar-10 (AC)	43	0	2.4	2.0	2.0	0	2.5
Yar-11 (AC)	57	0	2.4	2.0	2.3	2.3	3.5
Yar-82 (AD)	43	0	0	0	2.0	1.8	2.8
	57	0	0	0	2.5	2.0	3.5
Yar-90 (AC)	43	3.6	2.0	2.2	2.8	2.9	3.8

Discussion. Research in the field of molecular epidemiology of TE has indicated the existence of six genotypes of the TBE and has clarified the ranges of their occurrence [4]. Strains of the genotype 1, homologous to the prototypic Far Eastern Sofin strain, are relatively rare (16.4 percent of the population); they circulate predominantly in the Amur-Sakhalin region, as well as in the central, northwestern and western parts of the East European plain. Strains of the genotypes III and IV were found primarily in the territory of Siberia, Ural, Cisuralia, in the mountains of Central Asia and the Crimea [4]. The strains of genotype VI, genetically similar to the Central European Neudorfe strain (but not identical to it), dominate in Udmurtia, are detected in the Altay, in Western Siberia and in the western part of the East European Plain. Our research revealed that the Greek Vergina strain belongs to genotype VI. Thus, the range of occurrence of this genetic variant extends beyond the boundaries of Russia and includes the southern part of the TE range (Greece). On the other hand, the collected data indicate the possibility of circulation of Vergina-like strains in the territory of Russia. There was found to be a considerable similarity between the Vergina strain and a number of TBE strains isolated in Russia with respect to genetic, pathogenic, cultural and antigenic properties. With respect to a series of criteria, including antigenic properties, the Vergina strain is closest to the AC variant of the Yaroslavl strain Yar-90. In a study of the blood serum of the population of Yaroslavl Oblast in the NR there was found to be a dominance of an immune "interlayer" to the Vergina and Yar-90 strains (23.1 and 17.5 percent), whereas virus-neutralizing antibodies to the strains Sofin and Yar-173 were detected in 13.6 and 9.3 percent of the serum samples. In 8 of the 9 patients with encephalitis, exhibiting selective-strain seroconversion in the NR, antibodies only to the Vergina and Yar-90 strains were detected.

Table 5. Variants of Immune Response in TE Patients, Based on NR Data (Yaroslavl Oblast, 1991-1993)

Patient group, diagnosis	Number of patients*	Seroconversion to all strains	Selective seroconversion to strains				Stable titers of antibodies	Negative results
			Sofin (AC)	Yar-173 (AD)	Yar-90 (AC)	Vergina (AD)		
TE, meningeal and focal forms	14/20	7	0	0	1	4	2	6
TE, abbreviated form	5/8	0	1	0	1	2	1	3
ORVI, ORZ, Lyme disease, fever of unknown etiology	4/9	1	0	0	1	1	1	5
Total	23/37	8	1	0	3	7	4	14

*In numerator — number of patients with presence of specific antibodies; in denominator — total number of patients

Extremely limited information is available concerning the conditions for circulation of the Vergina serotype. In Greece there is widespread occurrence of the ticks *Ix. gibbosus* and *Rhipicephalus bursa* [12, 14]. The strain Yar-90, exhibiting a similarity to the Vergina strain, was isolated from a single specimen of the tick *Ix. persulcatus* [10], a species not encountered in Greece. In connection with the cited data the question arises as to how rigorously the TBE properties are associated with the species of carrier tick. At the present time increasingly more proof is being accumulated that the tick *Ix. persulcatus* is the carrier not only of the first (eastern) TBE subtype, but also other antigen variants, especially the Ayna/1448 serotype [1, 9], as well as the antigen variants isolated in Western Siberia, in Vologoda Oblast, Latvia [14]. The antigen singularity of the Vologoda TBE strains has been described in a number of studies [5, 6, 14], but in this case no comparisons with the Vergina serotype were made. A comparison of the available data with the results of our

research makes it possible to assume circulation in the northwestern region of a special antigen TBE variant differing from the Far Eastern TBE subtype and having a well-expressed relationship to the Vergina serotype. It also can be assumed that the spread of Vergina-like TBE strains in the territory of Russia is associated with the range of genotype VI of this virus.

Bibliography

1. Bochkova, N. G., Zhermer, V. Yu., Trukhina, A. G., et al., VOPR. VIRUSOL. (Problems in Virology), No 5, pp 572-575, 1985.

2. Dzhivanyan, T. I., Chunikhin, S. P., Lisak, V. M., et al., IBID., No 1, pp 92-96, 1986.

3. Zlobin, V. I., Drokin, D. A., Mansurov, P. G., et al., IBID., No 1, pp 24-27, 1991.

4. Zlobin, V. I., Molekulyarno-biologicheskoye opredeleniye i genotipicheskaya differentiatsiya virusa kleshchevogo entsefalita (Molecular Biology Determination and Genotypic Differentiation of Tick Encephalitis Virus), Author's summary of dissertation for award of degree of doctor of medical sciences, Moscow, 1992.

5. Izotov, V. K., Zhuravleva, M. G., Podelskiy, V. M., et al., in: Voprosy epidemiologii i prikladnoy immunologii (Problems in Epidemiology and Applied Immunology), Kazan, pp 69-72, 1975.

6. Izotov, V. K., Zhuravleva, M. G., Podelskiy, V. M., et al., IBID., pp 73-78.

7. Lyapustin, V. N. and Lashkevich, V. A., VOPR. VIRUSOL., No 1, pp 122-124, 1983.

8. Lyapustin, V. N., Lisak, V. M., Gritsun, T. S., et al., IBID., No 4, pp 419-427, 1985.

9. Pogodina, V. V., Bochkova, N. G., Korenskova, G. V., et al., IBID., No 6, pp 741-747, 1981.

10. Pogodina, V. V., Bochkova, N. G., Dzhivanyan, T. I., et al., IBID., No 2, pp 103-107, 1992.

11. Pogodina, V. V., Bochkova, N. G., Zlobin, V. I., et al., IBID., No 4, pp 158-162, 1993.

12. Papadopoulos, O., in: International Congress on Tropical Medicine and Malaria, 9th: Abstracts, Athens, p 32, 1973.

13. Papadopoulos, O., Arboviruses in the Mediterranean Countries, editors J. Vesenjak-Hirjan, et al., New York, pp 117-121, 1980.

14. Rubin, S. G. and Chumakov, M. P., IBID., pp 231-236, 1980.

15. Shumanin, V. A., Pletnev, A. G., Rubin, S. G. and Zlobin, V. I., J. GEN. VIROL., Vol 71, pp 1505-1515, 1990.

Russia: Organization of Mobile Structures in the Bloodstream: Functional Basis of Perfluorocarbon 'Artificial Blood'

964D0727A Moscow BIOFIZIKA in Russian Vol 41 No 1, Jan-Feb 96 pp 178-190

[Annotation and Article by G. R. Ivanitskiy, S. I. Vorobyev, Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, Pushchino, Moscow Oblast (manuscript received 17 Nov 95)]

[FBIS Translated Text]

Annotation

The example of Perftoran synthetic blood substitute is used to show that turbulent movement of emulsion microparticles in the bloodstream leads to the generation of dynamic microparticle chains. The chains are channels which transfer oxygen from the erythrocytes remaining after blood loss to tissues. Other aspects associated with the safety and effectiveness of perfluorocarbon blood substitutes are examined and a prognosis for their further development is made.

There are three ways of creating blood substitutes which have gas transport functions: perfluorocarbon blood substitutes,[1] free modified hemoglobin,[2] and hemoglobin capsulated in lipid vesicles (artificial erythrocytes).[3] This paper will examine the composition and properties of Perftoran, a synthetic perfluorocarbon emulsion used as a blood substitute with gas transport function. The creation of Perftoran was initiated in 1979 by F. F. Belopavlov and G. R. Ivanitskiy. The medical value of this product is great because it eliminates patient infection with AIDS, hepatitis, and other viral infections which can be found in donor blood. Moreover, industrial production of synthetic blood substitutes and group compatibility with blood of any patient makes them irreplaceable in rendering first aid in extreme situations (traffic and industrial accidents, military conflicts). However, the creation of perfluorocarbon blood substitutes was a more complex problem than initially imagined. Perfluorocarbons and surfactants induced side effects.

Over the course of five years many research groups in the USSR (and later Russia and the CIS) participated in work and pre-clinical trials of various emulsion recipes. In 1984 the Perftoran emulsion was created with a two-component perfluorocarbon composition. This emulsion demonstrated high effectiveness of gas transport function and had no toxicity or side effects.

Perftoran was admitted to clinical use because it successfully passed all stages of testing (I and II in 1984-1985, more than 600 patients; phase III in 1990-1995, more than 200 patients) and received the approval of the Pharmacological (22 Dec 94) and Pharmacopoeia (30 Aug 95) Committees of the Ministry of Public Health and the Medical Industry of the Russian Federation.

One may think the publication of this article strange in this thematic issue of the journal. The project to create Perftoran began three years after the death of Academician G. M. Frank and in essence seems to have no relation to the development of biophysical issues that he proposed. However, this is not so. Blood is always a test object of biophysicists. The program to study the mechanism of oxygen transport and the reaction of circulatory systems to external changes (pressure, nonionizing and later ionizing radiation) was formulated by G. M. Frank in 1934 in the organization of the Elbruss Expedition of the Academy of Sciences of the USSR,[4] and later in the development of atomic energy this program was supplemented and expanded, which is reflected in his works from 1934 to 1976.[5,6]

Thus, the creation of a synthetic perfluorocarbon blood substitute is based on many years of experience in studying hemodynamics and the reactions of blood to external effects. Moreover, the scientific school of Academician I. L. Knunyanets, which was conducted in our country in the 60s and 70s, took the world lead in the synthesis of perfluorocarbon compounds. The fusion of the school of biophysicists and chemists of fluororganic compounds laid the foundation in the early 80s for the appearance in the USSR after the death of G. M. Frank of a large-scale program, OTs 042, "Perfluorocarbons in Biology and Medicine,"[7] in the framework of which, among skepticism and opposition,[8] Perftoran was created (Table 1).

Table 1. Perftoran: Composition and properties.*PF = perfluorocarbon; **= All values wt/vol (%) to 100% volume of apyrogenic distilled water; *= Added before use.**

Composition		
Function	**Components**	
O_2 carriers	PF* -decalin	(13.0)**
	PF-methylcyclohexylpiperidine	(6.5)
Surfactant	Proxanol 268 (purified fraction of the active substance of plyuronik F-68, Mol. wt. <8000 Da	(4.0)
Low-molecular solution	NaCl (0.6), KCl(0.039), $MgCl_2$ (0.019), NaH_2PO_4 (0.02), $NaHCO_3$ (0.65), glucose (0.2), [$CaCl_2$ (0.003)***]	
Properties of Emulsion		
Function	**Controlled Parameter**	**Value**
Safety	LD_{50} for surfactant	14÷16 g/kg
	Concentration of free ion F	$<10^{-5}$ M
	Period of excretion, dose of 50 mg/kg	60÷90 days
	LD_{50} for entire product	140 ml/kg
Ion balance and osmotic pressure	pH	7.3 - 7.8
	Osmolarity	280-340 mOsm
O_2 capacity and O_2 transport	% by vol. O_2 (20°C)	7% by vol.
	% by vol. CO_2 (20°C)	60% by vol.
	Viscosity (25°C)	2.5÷3.0 cP

Composition		
Immune response	Neutropenic index	< 3
	Size of emulsion particles:	
	dispersion	< 0.3 μm
	\\average	0.07 μm
Storage time	without freezing (4÷8°C	> 30 days
	with freezing (-18°C)	> 3 years

Properties of Perfluorocarbon Emulsion, Determining Its Safety

In the 1970s after the papers of L. Clark, R. Geyer, R. Naito et al.[9-11] the idea "to create an effective blood substitute using perfluorocarbon" was taken up by many research groups around the world.

1. *The class of perfluorocarbon compounds is virtually infinite*, as is the class of organic compounds. One class corresponds to the other by replacing hydrogen with fluorine. Perfluorocarbons are slightly polar compounds in which the solubility of gases is increased as polarity decreases. The solubility of gases in pure liquid perfluorocarbons is about 50 percent by volume for O_2 and 200 percent by volume for CO_2.

2. *Perfluorocarbons are chemically inert substances*, because they are covered with a "coat" of fluorine covalently bound with carbon. The C-F binding energy is greater than C-H binding energy: for CH_3-F 119 kcal/mol, for CH_3-H 99 kcal/mol. The length of the bond for fluorine is also small, as is the case for hydrogen (binding length CH_3-H 1.09 Angstroms, for CH_3F 1.39 Angstroms). The replacement of hydrogen with fluorine leaves the volume of the molecule virtually unchanged, but makes the perfluorocarbon compound "rigid."[14] Perfluorocarbons do not inhibit the division of lymphoid cells in culture systems and do not produce chromosome aberrations in metaphasic cells. Perfluorocarbons can be used as a good substrate for culturing cells.[15]

3. *However, perfluorocarbons demonstrate biological activity on the molecular level*, interacting with cell membranes and receptors dissolved in lipids.[16,17,36] The surface tension of perfluorocarbons in most cases does not exceed 20 mN/m (20 dyne/cm). In liquid perfluorocarbons it is usually 10-20 mN/m, which indicates the extremely low value of their intermolecular interaction. Liquids with a surface tension above 20 mN/m do not wet the surface of perfluorocarbons, and liquid perfluorocarbons do not mix with them. We recall that the surface tension of water is 72 dynes/cm at 20,deg>. However, many oils and H-heptanes have a surface tension below 20 dynes/cm and liquid perfluorocarbons dissolve in them.[14] Thus, the hydrophobic/lipophilic index, that is, solubility in H-heptane and water, is an important indicator of perfluorocarbons characterizing both their rate of excretion from the body and the interaction with membranes and cell receptors. It should also be indicated that this index is temperature dependent.

4. *Other important indicators of perfluorocarbons are vapor pressure and boiling temperature.* These parameters characterize the rate of excretion of perfluorocarbons from the body. The period of half-excretion of perfluorocarbons studied for use in medicine varies from four days to several months. The lower the boiling point the faster perfluorocarbons are excreted through the lungs. However, it should be noted that there are many alternative paths of excretion, and not only in the form of exhaled vapor. Moreover, the desire (in pursuit of the excretion speed) to use perfluorocarbons with a low boiling temperature and a large vapor pressure may lead to undesirable physiological effects (to lung embolism and decompression syndromes, itching, tissue swelling).

5. *Perfluorocarbon compounds are approximately twice as heavy as water*, and as already noted, they are practically insoluble in water; thus, for blood substitutes one must prepare an emulsion of perfluorocarbons. Preparation of an emulsion requires surfactants. Otherwise the mixture will be poorly emulsified and instantly separate. Many compounds were tested as emulsifiers (animal and vegetable lipids, D-sorbitols, fatty acid salts, amino-oxides, block-copolymers, oxides of polyethylene and carbon). The selection was based on the last emulsifier. Plyuronik F-68, called Proxanol 268 domestically, was synthesized at the NIIOPIK [expansion not given]. When Plyuronik F-68 is purified well, it has a low toxicity and is excreted in the course of several hours. Moreover, this compound, in contrast to other surfactants, prevents hemolysis of erythrocytes, creates an insignificant colloid-osmotic pressure, and is a weak anticoagulant, lowering the viscosity of blood as well as increasing the effectiveness of the emulsion in conditions of fat embolism in the bloodstream. The price for

these advantages is increased thermodynamic instability of the emulsion.[36] Freezing is required for long-term storage.

6. Screening of many perfluorocarbons for their use in medicine has shown that *not one was fully optimal in the "medical effectiveness + safety" parameters system.* Thus, it was only natural to turn to the idea of creating two-component mixtures. This idea belongs to R. Naito's group (Green Cross Corp., Osaka) and was implemented by them in the Fluosol-DA blood substitute (FDA permission for clinical use, Jan 1990). However, as our studies have shown, one can improve its indicators by replacing one of the two perfluorocarbon components.

We replaced perfluortripropylamine with perfluorparamethylcyclohexylpiperidine (PMCP). This also required the addition of the appropriate surfactant and a change in the composition of the emulsion. The toxicity of our preparation was reduced by 15 percent and its efficiency of oxygen transport increased by a factor of 1.5. The excretion time (the price for these advantages) was increased by 25-30 percent. Moreover, the reactogenicity of the preparation was reduced, that is, its side effects. The physical parameters of the perfluorocarbons used and their chemical structure are presented in Table 2 and Figure 1.

Table 2. Physical Parameters of the Vapor of Liquid Perfluorocarbon Components Selected for the Perfloran Composition. *= perfluorocarbon decalin

No.	Parameter	PFD*	PMC P
1	Chemical formula	$C_{10}F_{18}$	$C_{12}F_{27}N$
2	Molecular mass, Da	462	595
3	Density (g/ml at 25°C)	1.938	1.920
4	Buoyancy of vapors (mm Hg at 37°C)	13	2.0
5	Boiling temperature (°C at 1 atm)	142	183-186
6	Viscosity (cP)	6.24	6.41
7	critical temperature of dissolution in H-hexane (°C)	22	38
8	Density of cohesion energy (kJ/m^3 at 25°C)	$18x10^{-4}$	$19.2x10^{-4}$
9	Molar heat of evaporation of pure liquid (kJ/mol at 25°C)	45.8+/-0.1	61.81+/-0.9
10	Molar volume (m^3/mol at 25°C)	$2.4x10^{4}$	$3.3x10^{-4}$
11	Percent solubility in water (% by vol. at 25°C)	$3x10^{-6}$	$2x10^{-7}$
12	Percent content of PMCP by weight in emulsion: PMCP/(PMCP + PFD) %	33.3	
13	Ratio of molecular surface of PFD to one molecule of PMCP	1:2.16	

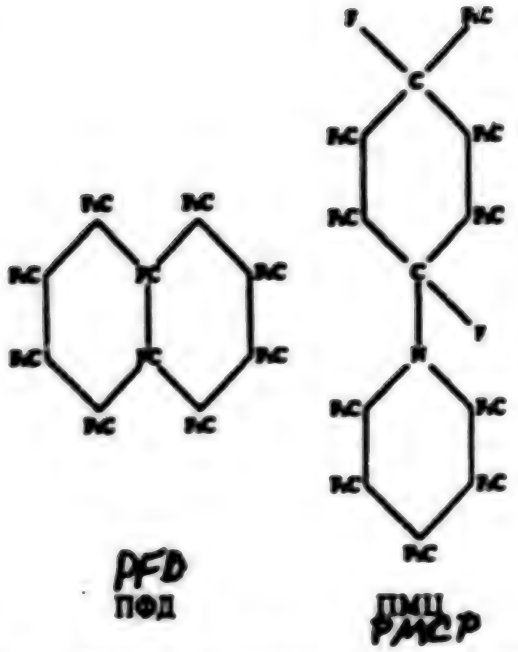


Figure 1. Chemical Structure of Perfluorocarbon Components Used in the Composition of Perftoran.

Key: PFD-perfluordecalin, PMCP-perfluorparamethyl cyclo hexylpiperidine.

7. *All preparations in the form of microparticles are to one degree or another reactogenic*, that is, they cause in some patients an immune system response similar to a flu (pain in the sacrum, chills, reddening of the skin, sometimes shortness of breath). This syndrome is also sometimes observed in intravenous administration of fatty emulsions without perfluorocarbon used for parenteral feeding, and for liposomes used for targeted delivery of medicines, as well as in blood loss during surgery.[13] These symptoms can be blocked by preparations such as indomethacin, dexamethasone or ibuprofen.[19-23]

In the introduction of foreign microparticles into the body stimulation of differentiation of stem cells should occur in the hemopoiesis system along the routes of lymphocytes and macrophages, which may appear as a temporary decrease in other formative elements. The blood is a reactive substation and the rate of renewal of formative elements is relatively high. The following are synthesized in a minute: 15×10^7 erythrocytes, 2×10^5 leucocytes, 2.5×10^5 thrombocytes. Nonetheless, the relative change in the formative elements over time occurs relatively slowly: lymphocytes are renewed in 8-10 hours, thrombocytes in 4 days, other leucocytes in 5 days, erythrocytes in 110-120 days. While the reaction (if it arises) to the introduction of microparticles into the bloodstream is almost instantaneous, the latent period does not exceed minutes. Consequently, the response of the immune system should have a trigger (launch) or avalanche mechanism. It has been noted[1] that this mechanism is associated not with differentiation processes on the cellular level, but with a triggered release of arachidonic acid during the phagocytic activity of macrophages on microparticles, leading to the release of thromboxanes and prostaglandins. Somewhat different is the version in Ref. 24 associated with the activation by surfactants of the blood plasma complement system and the release of so-called stress-proteins which aid on the one hand with phagocytic activity against microparticles, and on the other the generation of the preconditions for anaphylactic shock in relation to the appearance of anaphylatoxins, which also appears in the form of the aforementioned syndrome.[24,25] Moreover, the very process of puncturing a vein and introducing the preparation may cause a stress reaction.[24] These versions do not contradict one another, rather they are the links in one chain of events at the molecular and cellular levels. At the cellular level these events should lead not only to a temporary (slow) change in the blood formula, but also to a spatial (fast) redistribution of formative elements in the bloodstream and changes in the protein fraction of the blood.

It then follows that many quantitative indicators at the molecular or cellular level can be used as the index of reactogenicity of the preparation because they are correlated. We selected the neutropenic index J[24]: $J = C_n/C_r$, where C_n and C_r are respectively the content of neutrophils in the peripheral bloodstream after transfusion of the preparation containing microparticles, and the norm. This index is informative and reflects shifts in both the protein fraction associated with protein products of the activation of the blood plasma complement and the development of subsequent events in the chain of transitions to the cellular level of differentiation.[26,27] As such this index characterizes the fast spatial shift of neutrophils from the peripheral bloodstream and their collection in lung vessels. It was experimentally established that the maximum value of J should not exceed 2-3.[28,29] In the converse case the emulsion is reactogenic. Our studies showed that individually taken a 4 percent solution of surfactant, proxanol, does not have reactogenic properties.[26] in spite of the common opinion that it is associated with reactogenicity.

8. It was established that *an increase in the diameter of particles and an increase in the number of large-disperse particles in the emulsion increases the immune reaction* and the index J increases.[26,27] All of these studies make it possible to place the appropriate requirements on the sizes and dispersion of microparticles of the emulsion on

the technology of creating Perftoran in order to reduce the reactogenicity of the preparation (Figure 2).

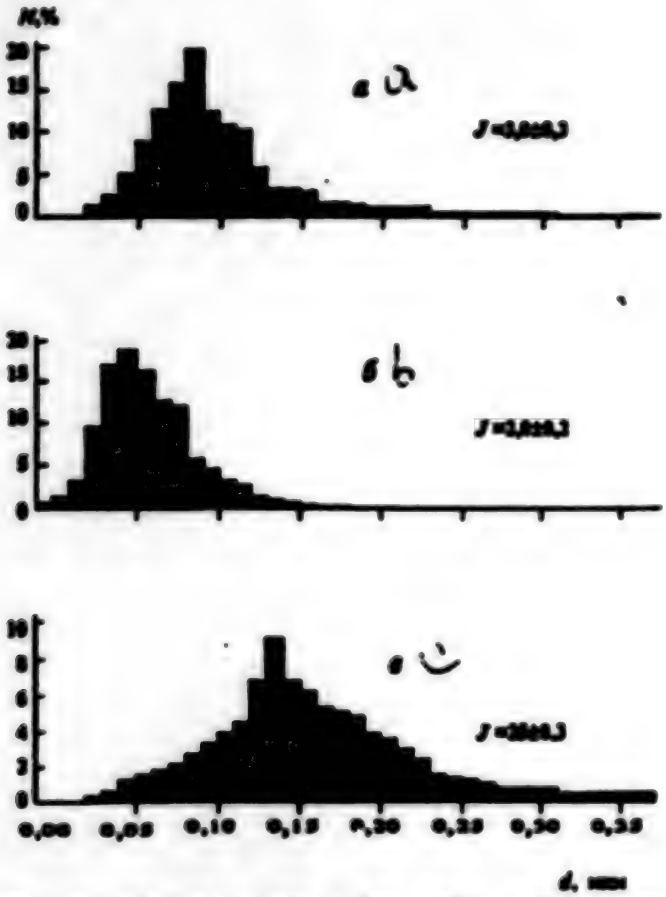


Figure 2. Distribution of Emulsion Particles by Size and the Effect of This Distribution on the Neutropenic Index (*I*).

Key: a. typical emulsion; b. emulsion after centrifuging (sedimentation at an acceleration of 14,2000g; c. emulsion after heating.[26,27] The x-axis is the diameter of the particles (*d*, μm, the y-axis is the relative number of particles, percent.

9. *The safety of Perftoran was shown in the process of pre-clinical studies.* The toxicity of Perftoran is low. A lethal dose in mice (in intravenous injection) was 200 ml/kg without plasma expander and 140 ml/kg in its full composition. Perftoran did not produce hemolytic effects in rats, dogs, or in human blood, was not pyrogenic, did not cause anaphylactoid reactions and did not inhibit hemopoiesis. In the process of pre-clinical studies the following were studied: its interaction with biological molecules and organoids, effect on ion transport through cell membranes, effect on the function of individual organs (heart, kidneys, brain) of rats and dogs in perfusion of the preparation through them. Its maximum toxicity was also determined in massive blood replacement (up to 70-90 percent of the blood volume). At doses of 20 ml/kg it was not teratogenic, not embryotoxic, not carcinogenic and does not cause pathological changes in the organs of animals.[30-38]

10. Moreover, *independent experts of the Alliance Pharmaceutical Corporation (Pharm. Cor. Alliance, San Diego, USA) used their own methods to study the preparation Perftoran in 1992.* Parameters indicated in Table 1 were verified. Also studied were its pulmonological effects, degree of thrombocytopenia and kinetics of body temperature change of rats after introduction of

the preparation under conditions of free behavior. The study was conducted with the aid of a telemetry system. After biological testing of Perftoran, the vice president of the Alliance firm, Doctor N. S. Faithfule, sent us the results of the analysis with the comment "It would seem that you have a very good emulsion."

How the Perfluorocarbon Emulsion Transports Oxygen

The oxygen capacity of the perfluorocarbon emulsion, compared with whole blood, is comparatively low (Figure 3). Blood with a 45 percent hemocrit dissolves at an oxygen pressure of P_{O_2} equal to 100 mm Hg 21 percent by volume O_2, and a 20 percent perfluorocarbon emulsion dissolves about 2-2.5 percent O_2. The oxygen capacity of the perfluorocarbon emulsion is a factor of 2-3 higher than in blood plasma and water. Nonetheless, it is clearly insufficient to maintain the cell metabolism of tissues. Moreover, the characteristic of oxygen saturation of hemoglobin has an S-shape, and saturation of the perfluorocarbon emulsion with oxygen has a linear characteristic. However, the opinion that hemoglobin as a chemical binder of O_2 in itself has a high oxygen capacity is overestimated. One gram of hemoglobin can bind a maximum of 1.38 ml of O_2, while, for example, one gram of iron (if it forms ferrous oxide) can bind 300 ml of O_2 (Ref. 37).

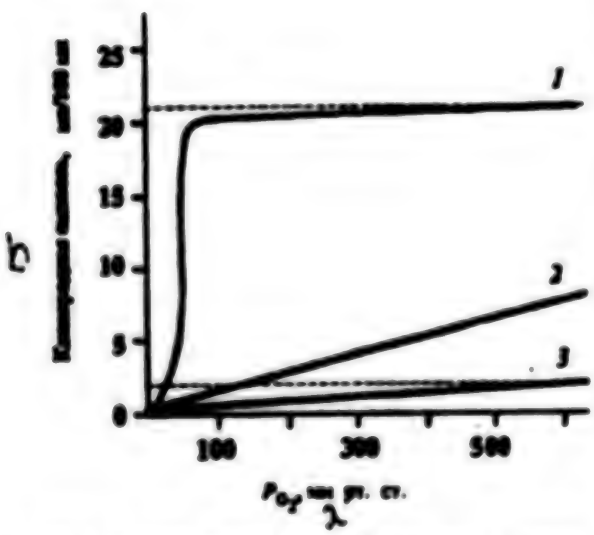


Figure 3. Oxygen Capacity as a Function of Oxygen Pressure P_{O_2}

Key: 1. for whole blood (45% hemocrit); 2. Perftoran 20% by vol/wt; 3. blood plasma. a. P_{O_2}, mm Hg; b. Oxygen capacity, ml/100 ml.

The efficiency of O_2 transport with hemoglobin is low. The heavy hemoglobin molecule, which weighs about 70 kDa "carries" per circulation cycle a total of four O_2 molecules with a eight of 128 Da, which is only 0.2 percent of the weight of the transporting molecule. Manifesting great wastefulness in its transport system, nature made up for it with cooperative effects in the regulation system (loading and unloading of oxygen).[36] Hemoglobin loads and unloads its oxygen in a narrow range of changes in gas pressure in the medium (from 0 to 100 mm Hg). The rate of loading/unloading is pH-dependent, and varies by a factor of ten as pH changes. At pH 7.26 the transition time from hemoglobin to oxyhemoglobin is 40-80 ms, and at pH 7.4 it is 300 ms.[36] The oxygen capacity of 1 l of blood is the same as 1 l of air, that is, due to hemoglobin the entire organism becomes "transparent" to oxygen and the internal organs have the potential possibility (if it is realized) of obtaining the same "allowance" as the external organs.

The low oxygen capacity of the perfluorocarbon emulsion somehow provided a basis for the speculative assertion that the perfluorocarbon emulsions were ineffective for oxygen transport. Let us present a typical statement which has been repeated in various ways in the literature: "The present ineffectiveness of the use of the first generation of perfluororganic compound emulsions as a blood substitute and oxygen carrier is evidenced, for example, by the data of Tremper et al. (1984) which indicate that in clinical use of a 20 percent by weight/volume emulsion of Fluosol-DA in a dose of 20 ml/kg the fluorocrite is approximately 3 percent, which corresponds to 0.5 g% hemoglobin. It is difficult to imagine that an additional 0.5 g% hemoglobin could have a significant effect on the oxygen and hemodynamic status of the patient."[39] As a result of this assertion some researchers increased the content of perfluorocarbon particles in circulation by increasing the concentration of the emulsion.[40] The effect was the opposite of the expected: the oxygen transport into the tissues was reduced.[40] As will be shown below the assertion about the ineffectiveness of the emulsion was based on careless reasoning associated with the substitution of the concept of "oxygen transport" with "oxygen capacity."

Oxygen transport is the diffusion flux of oxygen into tissue. The oxygen flux i is in no way linked with the oxygen capacity, and is defined in accordance with Fick's law by the coefficient of diffusion of oxygen $D$and the difference in oxygen potentials between the blood and tissue ($U_{bl} - U_{tis}$):

$$i = D(U_{bl} - U_{tis}$$

Fick's law is a complete analogy of Ohm's Law. Let us explain this statement with an elementary model of electric circuits. Let us assume that we have a small electric motor and an electric battery. Let us connect the motor with a copper wire to the battery. It is obvious that the current flowing in the circuit will be

determined by the voltage at the battery terminals and the conductivity of the circuit (the inverse quantity: the internal resistance of the battery + the resistance of the wire + the resistance of the motor windings). The current does not depend on the battery capacity, but the length of operation of the motor does. If we increase the charge on the battery, by replacing it with a new one, the motor will work as long as we wish. Now we connect the motor to the battery not with a copper wire, but for example, with a glass fiber. All the voltage will be dissipated in the fiber because the conductivity of the glass is low and the motor will not be able to perform work, independent of the capacity of the batter connected to the circuit. This model has obvious correlations with the real gas transport system in an organism. The battery is the erythrocyte; the motor is the mitochondria of the tissue cells; the rate of replacement of the battery is the rate or per minute volume of circulation; the battery discharge is determined by the arterial-venous (A-V) difference in the oxygen capacity in the "erythrocytes + blood plasma" system; the connecting wire with a high conductivity (copper in our example) corresponds to direct contact of the erythrocyte membrane with the arteriole wall and capillary vessels, and the wire with a low conductivity (glass in our example) corresponds to the transfer of oxygen through the blood plasma (water). The latter situation is typical when blood loss is replaced with traditional blood substitutes without a gas transport function (Ringer and Tyrode solutions, polyglucin, gelatinol, lactosol, blood plasma, etc.), but is absolutely different for perfluorocarbon emulsion blood substitution:

1. *The conductivity of oxygen by pure perfluorocarbon compared with water is high.* The solubility of oxygen in perfluorocarbon is up to 50 percent by volume, and for water, only 2 percent, that is, a factor of 25 lower. Thus, if a chain of particles touching each other forms in the perfluorocarbon emulsion, the conductivity of oxygen rises and consequently, the flow of O_2 from the erythrocyte increases as a source with a high partial oxygen pressure in the tissue (Figure 4).

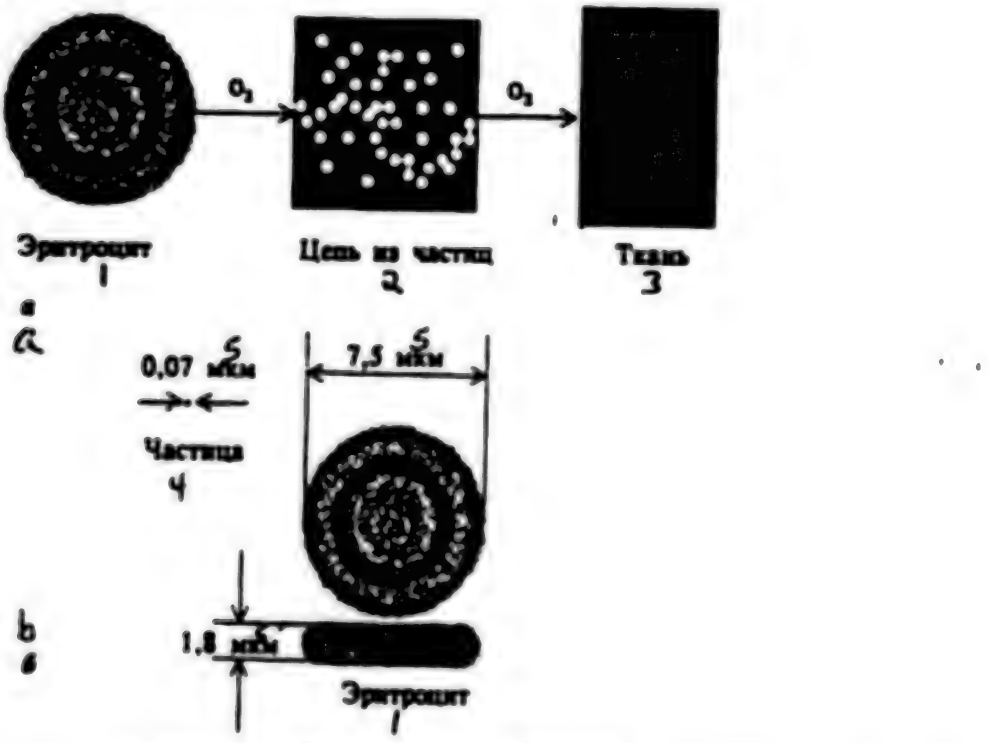


Figure 4. Mechanism of Oxygen Transport.

Key: —a. organization of oxygen transport from the erythrocyte into the tissue with formations of perfluorocarbon particles in chain-O_2 channel circulation; —b. size of emulsion particles and erythrocyte. —1. erythrocyte; —2. chain of particles; —3. tissue; —4. particle; —5. μm.

2. *Erythrocytes screened by water never completely give up their oxygen charge.* The arterial-venous oxygen difference, even for high physical loads, does not increase by more than 30 percent. Thus, 20-30 percent

of the erythrocytes, if they were to fully yield their oxygen charge to the tissue (A-V → A) would suffice for normal functioning of the organism. However, this not only doesn't occur, on the contrary in the breakdown of erythrocyte structures like coin-shaped columella the screening of erythrocytes by water increases and the oxygen yield worsens. The venous oxygen capacity increases, it does not fall. Oxygen is dissolved in the plasma, but it is not transferred to the tissue. As V. S. Yarochkin correctly points out,[40] "hypoxia occurs during hyperoxia:" the capacity of oxygen in the plasma is high, and the flux of oxygen into the tissues is insignificant.

3. We have shown[41] that the probability of the formation of chain channels of O_2 of microparticles in blood plasma is proportional to $v\rho/r^2\mu$, were v, ρ, and r are respectively the rate of blood flow, and the density and radius of emulsion microparticles. The quantity μ is the static viscosity which is proportional to rC^2/α, where C is the concentration of particles in the bloodstream, α is the coefficient of mobility of particles in water. Thus, *an increase in concentration of perfluorocarbon particles in the bloodstream will lead to an increase in blood viscosity after replacement and will not improve, but rather will worse gas transport.* An important indicator of the quality of the emulsion is not the absolute O_2 capacity, but the dynamic capacity, which is equal to the quotient of the division of absolute capacity by viscosity. Perftoran has a low viscosity, less than 3.0 cP (Table 1). The perfluorocarbon emulsions created by various foreign research groups are compared by this criterion in Ref. 42.

4. Obviously, the size and dispersion of sizes of particles play an important role in the frequency of channel formation for the reason indicated in section 3. *The conductivity of the channels that are formed is defined by the surface of the contacting particles.* The relative sizes of particles and the erythrocyte are shown in Figure 4b. The ratio of their surfaces for equal total volumes is $6x10^3$. Thus, particles moving in the bloodstream may create in the dynamics simultaneously a colossal amount of channels while keeping the surface of the erythrocytes at the walls of the vessels.

5. *One of the experimental results with rat liver mitochondria*[43,44] *demonstrating the effectiveness of perfluorocarbon emulsions in blood replacement is shown in Figure 5.*

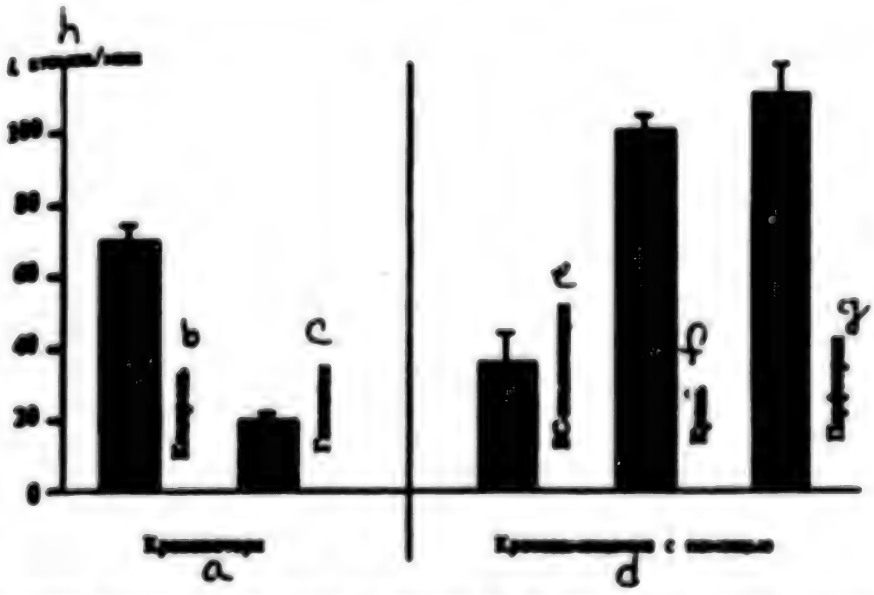


Figure 5. Relative Value of Oxygen Flux (rate of oxidation of substrates), Measured in Mitochondria of Rat Liver Cells After Blood Letting and Blood Replacement: protein-salt composition intrinsic to blood and Perftoran.[43]

Key: —a. Blood loss; —b. control; —c. hypoxia; —d. Blood replacement with: —e. protein-salt composition; —f. blood; —g. Perftoran; —h. *i*, atoms/minute.

The quantity of O_2 flux was defined by the change in the rate of oxidation of various mitochondrial substrates.[46] The rate of oxidation in turn was measured polarographically with a Clark electrode. Another example is Ref. 47. In rabbits with implanted platinum electrodes the amount of O_2 was measured in brain tissue during infusion of six types of perfluorocarbon emulsions. As one would expect, the increase in O_2 in brain tissue did not correspond to the low total level of oxygen capacity of plasma in the bloodstream and the indicators of O_2 solubility in the perfluorocarbon emulsion. The results and clinical use of Perfloran are presented in Refs. 35 and 36.

Price, Demand, and Development of Perfluorocarbon Blood Substitutes

Amidst the broad area of sue of artificial blood substitutes one can indicate key areas, for example, heart failure, heart attack, insult and hemorrhagic shock, but primarily, surgical use of blood substitutes.

1. *The international cost of the portion of donor blood used for one transfusion is continuously rising* and in 1995 varied, depending on blood group, from 150 to 200 US dollars. For patients the cost of one transfusion (400 ml) due to additional testing and additional costs, usually varies from 300 to 400 dollars. This price is determined not only by the cost of blood but also the need for multiple tests (Table 3).[44]

Table 3. Chronology of Discoveries of Pathological Agents in the Blood and the Creation of Methods to Monitor the Quality of Donor Blood.[44]

Year	Discovery	Pathology
1905	Discovery of the agent for pallid Treponema (1905). Creation of monitoring method	syphilis
1971	Discovery in 1964 of the antigen of the hepatitis B virus. Development of methods to detect it based on a surface antigen	hepatitis
1983	Discovery of the human immunodeficiency virus (HIV)	AIDS
1985	Discovery of the VCM virus (1956), creation of methods to monitor its presence based on antibodies	cytomegaloviral infection
1985	Step-by-step industrial production of tests to detect anti-HIV1 antibodies. Suppression of viruses by thermal fractional coagulation	AIDS
1986	Detailed description of the process of infection of erythrocyte with merozoites (1969). Detection of agents with plasma dialysis	fever (malaria)
1987	Creation of methods to detect various types of viruses. Development of a solvent-purifiers coagulating viral particles	AIDS, hepatitis, other hidden viruses
1988	Creation of a method of epidemiological study of viral hepatitises in potential donors; evaluation of the rate of appearance of viruses and the creation of preventive methods	hepatitis-new type
1989	Creation of methods to detect AIDS agents by identification of mixed forms HALVE 1 and 2	AIDS
1990	Identification of the genome of the hepatitis C virus (1988) and the creation of second-generation tests for its diagnosis based on antibodies	hepatitis C
1991	Structural proteins of the HCV virus obtained and used to detect antibodies. Second-generation technology	hepatides
1992	Determination of risk factors of transfer of infection from donor blood associated with retroviruses and hepatitises. Creation of antibody systems	AIDS, hepatides, and other viruses

2. *The need for blood transfusions is enormous* and is about one transfusion per 50-100 persons per year. Thus, for Russia alone the potential need is about 1 million liters of blood substitutes per year. The hindering factor is financial limitations. According to the data of the Hema Gen company,[45] the potential world market for synthetic blood substitutes for use in cardiopulmonological surgery, hemodilution, and traumatology varies between 1.9 and

2.9 billion US dollars for a calculated cost of 400 dollars per dose. The prognosis for the market being filled by firms known to us is presented in Table 4.

Table 4. Prognosis for Market for Perfluorocarbon Blood Substitute Preparations With Gas Transport Function Being Filled.

No.	Clinical approval and prognosis for production of preparation	Name of preparation	Basis of gas transport carrier	Firm
1	Received permission for clinical use (FDA 8 Jan 1990), commercial preparation	Fluosol DA	Perfluorodecalin and perfluoctripropylamine	Green Cross Corp., Osaka, Japan and Alpha Therapeutik, USA
2	Obtained permission for clinical use (Pharmacological Committee of the Russian Federation 2 Dec 1994). Prognosis of release of commercial preparation 1996	Perftoran	Perfluorodecalin and perfluoroparamethylcyclohexylpiperadine	Perft cross joint stock pharmaceutical firm, Pushchino, Russia
3	Second phase of clinical testing (prognosis for release of commercial preparation 1996)	Oxygent	Perfluorooctylbromide	Alliance Pharmaceutical Corp., San Diego, CA, USA
4	Second phase of clinical testing (prognosis for release of commercial preparation not reported)	Oxyfluor	Perfluorodichlorooctane	Hemo Gen/PFC., St. Louis, MO, USA

3. The prospects for further development of perfluorocarbon blood substitutes are not favorable (one cannot plan new discoveries). Nonetheless, given the experience we have accumulated in fifteen years we can try to make predictions on a qualitative level. *Three scenarios are possible for the creation of the next generations:*

1) synthesis of some perfluorocarbon compound which is ideal in all parameters as the basis of a blood substitute will succeed. The probability of this is very small;

2) the indicators of Perftoran as a two-component mixture will not be surpassed. The probability of this scenario is higher than the previous one, but is still small;

3) finally, the creation of new two or more component compositions from various perfluorocarbons will succeed which will make up for the drawbacks of some with the advantages of others. This is the most likely scenario.

The authors would like to thank the Central Military-Medical Administration of the Ministry of Defense of the Russian Federation, the Ministry of Public Health and the Medical Industry of the Russian Federation, The Russian Academy of Sciences, the Russian Academy of Medical Sciences, all stockholders of the Perftoran pharmaceutical firm, the many participants in program OTs 042, "Perfluorocarbons in Biology and Medicine", chemists, physicists, biologists, and physicians, as well as the Russian Fund for Fundamental Research, for their material, intellectual and moral support of the research leading up to the creation of Perftoran, and we hope for help and collaboration in the further development of research in the subject "Perfluorocarbons in Biology and Medicine."

References

1. J. G. Riess, ARTIF. ORG. Vol 14, 1991 p 255.

2. T. M. S. Chang, R. P. Geyer, eds., *Blood Substitutes* NY: Dekker, 1989.

3. K. C. Lowe, ed., *Blood Substitutes: Preparation, Physiology,and Medical Applications* Chichester: Ellis Horwood, 1988.

4. G. M. Frank, IZV. AN SSSR Vols 4-5, 1939 p 363.

5. G. M. Frank, *Biofizika zhivoy kletki. Izbrannyye trudy* [Biophysics of the Live Cell. Selected Works] Moscow: Nauka, 1982.

6. G. M. Frank, *Dokl. Mezhdunar. konf. po mirnomy ispolzovaniyu atomnoy energii "Deystviye oblucheniya na organizm* [Proc. International Conf. on the Peaceful Use of Atomic Energy "Effect of Radiation on an Organism"] Moscow: Izd-vo AN SSSR, 1955 p 112.

7. G. R. Ivanitskiy, F. F. Beloyartsev, *Perftoruglerody v biologii i meditsine v SSSR* [Perfluorocarbons in Biology and Medicine in the USSR] Pushchino: ONTI NTsBI, 1982.

8. G. R. Ivanitskiy, *Kto ubil professora F. F. Beloyartseva? Istoriya "goluboy krovi" v kaleydoskope pressy* [Who Killed Professor F. F. Beloyartsev? The Story of "Blue Blood" in the Caleidoscope of the Press] Moscow: Izd-vo Vivasvat, 1994.

9. L. S. Clark, Jr., F. Gollan, SCIENCE Vol 152, 1966 p 1755.

10. R. P. Geyer, NEW ENGL. J. MED. Vol 289, 1973 p 1077.

11. R. Naito, K. Yokoyama, *Proc. Tenth Int. Congr. Nutr. Symp. PFC Artif. Blood* Kyoto, 1975 p 55.

12. K. C. Lowe, ADV. MATER. Vol 3, 1991 p 88.

13. J. G. Riess, VOX SANG. Vol 61, 1991 p 225.

14. M. Matsuo, S. Otosi, *Soyedineniya ftora* [Fluorine Compounds] Moscow: Mir, 1990 p 157.

15. G. R. Ivanitskiy, V. V. Arkhipov, F. F. Beloyartsev, E. I. Lezhnev, DAN Vol 28 No 1, 1981 p 225.

16. Yu. M. Kokoz et al., DAN Vol 270, 1983 p 459.

17. S. I. Vorobyev, G. R. Ivanitskiy et al., DAN Vol 299, 1988 p 228.

18. R. Lustig et al., RAD. ONCOL. BIOL. PHYS. Vol 16, 1989 p 1587.

19. R. G. Evans et al., RAD. ONCOL. BIOL. PHYS. Vol 19, 1990 p 415.

20. R. F. Mattrey, RADIOLOGY Vol 170, 1989 p 18.

21. J. N. Bruneton et al., RADIOLOGY Vol 170, 1989 p 179.

22. H. O. Shuberth, A. Wretlind, ACTA CHIR. SCAND Vol 278, 1961 supp. 3-12.

23. W. G. Teague et al., PEDIT. RES. Vol 22, 1987 p 714.

24. N. N. Pyatkovskaya et al., *Perftoruglerodnyye aktivnyy sredy dlya meditsiny i biologii* [Perfluorocarbon Active Media for Medicine and Biology, Pushchino: 1993 p 167.

25. W. Vogt, TRENDS PHARMACOL. SCI. Vol 6, 1985 p 114.

26. S. I. Vorobyev et al., BIOSOVMESTIMOST Vol 3, 1995 p 51.

27. S. I. Vorobyev et al., BIOMATERIAL-LIVING SYSTEM INTERACTIONS Vol 3, 1995 p 45.

28. S. I. Vorobyev, G. R. Ivanitskiy, K. N. Makarov et al., *Perftoruglerodnyye aktivnyye sredy dlya meditsiny i biologii* [Perfluorocarbon Active Media for Medicine and Biology] Pushchino, 1993 p 33.

29. S. I. Vorobyev, G. R. Ivanitsky, "Perfluorocarbon Emulsion Stabilized by Proxanol" Pushchino, 1994 18 pp.

30. F. F. Beloyartsev, ed., *Mediko-biologicheskiye aspekty primemeniya emulsiy perftoruglerodov* [Medical-Biological Aspects of the Use of Perfluorocarbon Emulsions] Pushchino, 1983 185 pp.

31. F. F. Beloyartsev, ed., *Perftorirovannyye uglerody v biologii i meditsine* [Perfluorided Carbons in Biology and Medicine] Pushchino, 1980 182 pp.

32. F. F. Beloyartsev, ed., *Ftoruglerodnyye gasperenosyashchiye sredy* [Fluorocarbon Gas Transfer Media] Pushchino, 1984 182 pp.

33. G. R. Ivanitskiy, S. I. Vorobyev, eds., *Perftoruglerodnyye aktivnyye sredy dlya meditsiny i biologii (novyye aspekty issledovaniya)* [Perfluorocarbon Active Media for Medicine and Biology (New Aspects of Research)] Pushchino, 1993 242 pp.

34. A. M. Golubev et al., *Reaktsiya biologicheskikh sistem pri zameshchenii krovi emulsiyami ftoruglerodov* [Reaction of Biological Systems in Replacement of Blood with Fluorocarbon Emulsions] Moscow: TEIS, 1993 137 pp.

35. G. R. Ivanitskiy, S. I. Vorobyev, eds. *Fiziko-khimicheskiye i klinicheskiye issledovaniya perftoroorganicheskikh soyedineniy* [Physicochemical and Clinical Studies of Perfluororganic Compounds] Pushchino, 1994 117 pp.

36. G. R. Ivanitskiy, S. I. Vorobyev, eds., *Fiziologicheskaya aktivnost ftorsoderzhashchikh soyedineniy (eksperiment i klinika)* [Physiological Activity of Fluoride-Bearing Compounds (Experiment and Clinical Studies)] Pushchino, 1995 246 pp.

37. K. P .Ivanov, FIZIOL. ZHURNAL IM. SECHENOVA Vol 78 No 11, 1992 p 11.

38. M. Moshizuki, Japan. J. PHYSIOL. Vol 16, 1966 p 635.

39. A. A. Bayev, VESTN. AKADEMII NAUK Vol 6, 1989 p 55.

40. V. S. Yarochkin, "Physiological Activity of Fluoride-Bearing Compounds Experiment and Clinical Studies), ed. G. R. Ivanitskiy, S. I. Vorobyev, 1995 p 107.

41. G. R. Ivanitskiy, S. I. Vorobyev, "Perfluorocarbon Active Media For Medicine and Biology (New Aspects of Research) edited by G. R. Ivanitskiy, S. I. Vorobyev, Pushchino, 1993 p 5.

42. S. I. Vorobyev, G. R. Ivanitskiy, K. N. Makarov, V. V. Arkhipov, "Physiological Activity of Fluoride-Bearing Compounds (Experiment and Clinical Studies) edited by G. R. Ivanitskiy, S. I. Vorobyev, Pushchino, 1995 p 33.

43. F. F. Beloyartsev et al., "Ftorosan—oxygen-carrying Perfluorochemical Plasma Sustitute" Pushchino, 1983 19 pp.

44. C. Janot, A.-M. Courouce, LA RECHERCHE Vol 24 No 254, 1993 p 618.

45. G. Dutton, GENETIC ENG. NEWS Vol 1, 1995 p 6.

46. N. N. Burstovetskiy, Ye. I. Mayevskiy, "Perfluorided Carbons in Biology and Medicine" edited by F. F. Beloyartsev, Pushchino, 1980 85 pp.

47. C. Lenard et al., BIOMATER. ARTIF. CELLS and ARTIF. ORGANS Vol 16 No 1-3, 1988 p 375.

This is a U.S. Government publication produced by the Foreign Broadcast Information Service (FBIS). Its contents in no way represent the policies, views, or attitudes of the U.S. Government.

FBIS collects, translates, disseminates, and analyzes foreign open-source information on behalf of the U.S. Government. Its publications may contain copyrighted material. ***Copying and dissemination is prohibited without permission of the copyright owners.***

— Bracketed indicators before the first sentence of each item describe the way in which the material was processed by FBIS.

— Headlines and all bracketed explanatory notes are supplied by FBIS.

— Personal and place names are rendered in accordance with the decisions of the U.S. Board on Geographic Names as adapted by FBIS. Unverified names in radio and television material appear in parentheses and are spelled phonetically; words and phrases in parentheses preceded by a question mark are unclear in the original and deduced from context.

SUBSCRIPTION INFORMATION

U.S. Government Customers

For a list of FBIS products, to subscribe to an FBIS publication, or to indicate a change of address contact:

FBIS
P.O. Box 2604
Washington, DC 20013-2604
Telephone: (202) 338-6735
FAX: (703) 733-6042

Non-Government Customers

Subscriptions are available from the National Technical Information Service:

NTIS
5285 Port Royal Road
Springfield, VA 22161
Telephone: (703) 487-4630
FAX: (703) 321-8547

New subscribers should expect a 30-day delay in receipt of the first issue.

END OF FICHE

DATE FILMED

18 July 96